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Functional Outcome after Free Flap Reconstructions in Oral and Pharyngeal Cancer

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Academic dissertation
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To Veli-Matti,
Ella, and Kalle

Abstract

Oral cancer ranks significantly among the ten most common cancers worldwide. Since oral cancer is commonly diagnosed at locally advanced stage, curing the cancer demands extensive tissue resection. The emergent defect is reconstructed generally with a free flap transfer. Modern reconstruction techniques aim at attaining optimal function. The oral functions of breathing, speaking, chewing, and swallowing are vital and essential for an individual. Repair of the upper aerodigestive track with maintenance of its multiform activities is challenging. Comprehensive studies on function advance the improvement of the treatment outcomes.

Fifty consecutive patients having undergone free flap reconstruction for oral, oropharyngeal, or hypopharyngeal cancer between 1989 and 1995 were analyzed retrospectively for postoperative survival and complications. Forty-four similar consecutive patients were prospectively followed-up between 1996 and 1999 and analyzed for postoperative survival and complications. Their functional outcome was also determined in terms of quality of life, speech, swallowing, and intraoral sensation. The parameters were measured preoperatively, and at four time points during a follow-up period of 12 months. The instrument used in quality of life assessment was the University of Washington Head and Neck Questionnaire. Speech was analyzed instrumentally for aerodynamic parameters as well as for nasal acoustic energy. Speech was also assessed perceptually for articulatory proficiency, voice quality, and intelligibility. Videofluorography was performed to determine the swallowing ability with various bolus consistencies. Intraoral sensation was measured by moving 2-point discrimination.

The 3-year overall survival after microvascular free flap reconstruction was 42% (Study I) and 45% (Study II). In the follow-up study (II), the 1-year disease-free survival was 43%. Postoperative complications arose in 58% (Study I) and 66% (Study II) of the patients. Flap success rate was 96% (Study I) and 98% (Study II). Perioperative mortality varied between 2% (Study I) and 11% (Study II). Unemployment and heavy drinking were the strongest predictors of survival. Unemployment and heavy drinking increased the risk of dying 4.4-fold and 2.4-fold, respectively. The global quality of life score deteriorated after the operation and did not return to the preoperative level during the follow-up. Significant reduction was detectable in the domains measuring chewing and speech, and in appearance and shoulder function. The result highlights the importance of the functional outcome of the treatment. The basic elements necessary for normal speech were maintained. Perceived articulatory and vocal dysfunction, however, particularly when co-occurring, carry a risk for speech intelligibility. Oral nutrition was almost always re-established although swallowing often proved impaired and unsafe. Sensation weakened but was unrelated to oral functions.

Contents

List of original papers

This thesis is based on the following articles:

I Markkanen-Leppänen M, Suominen E, Lehtonen H, Asko-Seljavaara S. Free flap reconstructions in the management of oral and pharyngeal cancer. *Acta Otolaryngol* 2001;121:425-429.

II Markkanen-Leppänen M, Mäkitie AA, Haapanen M-L, Suominen E, Asko-Seljavaara S. Quality of life after free-flap reconstruction in patients with oral and pharyngeal cancer. *Head Neck* 2006;28:210-216.

III Markkanen-Leppänen M, Isotalo E, Mäkitie AA, Suominen E, Asko-Seljavaara S, Haapanen M-L. Speech aerodynamics and nasalance in oral cancer patients treated with microvascular transfers. *J Craniofac Surg* 2005;16:990-995.

IV Markkanen-Leppänen M, Isotalo E, Mäkitie AA, Rorarius E, Asko-Seljavaara S, Pessi T, Suominen E, Haapanen M-L. Swallowing after free-flap reconstruction in patients with oral and pharyngeal cancer. *Oral Oncol* (in press).

V Markkanen-Leppänen M, Isotalo E, Mäkitie AA, Asko-Seljavaara S, Pessi T, Suominen E, Haapanen M-L. Changes in articulatory proficiency following microvascular reconstruction in oral or oropharyngeal cancer. *Oral Oncol* (in press).

The papers are referred to in the text by their roman numerals. The publishers of the original papers have kindly granted permission to reprint the articles.

Abbreviations

CT .... Chemotherapy
DFS.............................. Disease-free survival
DSS.............................. Disease-specific survival
H&N .... Head and neck
HP............................... Hypopharyngeal, hypopharynx
LUFF .... Lateral upper arm free flap
Nasa0 .... Nasal cross-sectional area
Nasar............................ Nasal airway resistance
OC .... Oral cavity
OP .... Oropharyngeal, oropharynx
OS................................ Overall survival
PREOP .... Preoperative, preoperatively
POST6wk...................... 6 weeks postoperatively
POST3mo .... 3 months postoperatively
POST6mo .... 6 months postoperatively
POST12mo................... 12 months postoperatively
QOL............................. Quality of life
RFFF .... Radial forearm free flap
RT .... Radiotherapy
SCC .... Squamous-cell carcinoma
Sp-UWQOL .... Speech according to the University of Washington quality of life questionnaire
Sw-UWQOL................. Swallowing according to the University of Washington quality of life questionnaire
UADT .... Upper aerodigestive track
UWQOL .... University of Washington quality of life questionnaire
VFG............................. Videofluorography
VP................................ Velopharyngeal, velopharynx
VP0.............................. Velopharyngeal orifice area

1 Introduction

Malignant tumors in the head and neck (H&N) region account for approximately 5% of all the cases of cancer diagnosed annually. Of total cancer, oral (= oral cavity) and pharyngeal cancer encompass about 2.5% and 1.2%, respectively (Parkin and Bray, et al., 2005). Over 90% of oral and pharyngeal cancers are squamous-cell carcinomas (SCC). These cancers are related to lifestyle and lower socioeconomic status, and they occur more often in the developing countries than in the developed world (Scully and Bedi, 2000; Scully and Porter, 2000; Walker, Boey, and McDonald, 2003). Oral and pharyngeal cancer cause significant losses to human and financial capital.

Oral or pharyngeal cancer often arise in a place hidden from the view and manifests with unspecific symptoms. Owing to these insidious characteristics, diagnostic delay is common (McGurk, and Chan, et al., 2005; Scott, Grunfeld, and McGurk, 2005). These cancers are frequently discovered only after having become locally advanced and disseminated into the regional lymph nodes. Therefore, treatment of cancer threatens the face and the voice, which are characteristics crucial for individual identity. Management of high stage tumors generally demands a combination of treatment modalities, typically surgery and radiotherapy (RT). Modern reconstruction techniques enable voluminous tissue ablations. Reconstruction of the upper aerodigestive track (UADT) faces particular challenges because of the need for maintenance of the multiform functions in this area, i.e., breathing, speaking, chewing, swallowing, and of the facial appearance. UADT functions are vital for an individual and central for one's quality of life (QOL). Furthermore, the treatment outcome is plainly visible.

Despite therapeutic advances in oral and pharyngeal cancer, survival has not shown clear improvement. The 5-year overall survival rate has been about 50% for the past several decades (Scully and Bedi, 2000; Walker, Boey, and McDonald, 2003; Lavelle and Scully, 2005). In addition to improving the survival rate, an objective and challenge for research include development of treatment protocols that spare organs and functions by maximally reducing treatment toxicity. In the future, ideal solutions for the care and cure of oral and pharyngeal cancer may be enhanced with the aid of molecular biology (Weir, 2000; Lavelle and Scully, 2005). Meanwhile, the present treatment methods, such as the labor-intensive microvascular reconstructions, require critical assessment in order to evaluate and improve the efficacy of the treatment strategies.

2 Review of the literature

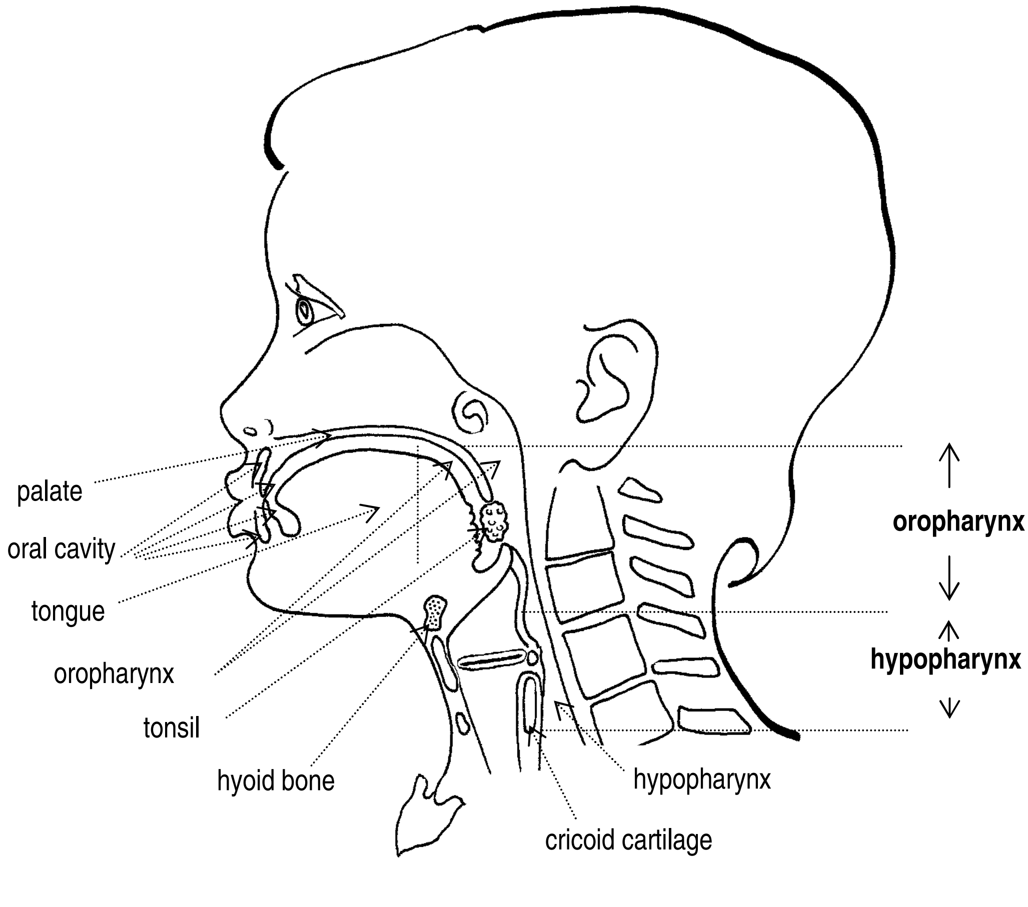
2.1 Epidemiology of oral and pharyngeal cancer

Worldwide projections indicate that in 2005, 430,000 new oral and pharyngeal SCC are diagnosed (Scully and Bedi, 2000; Walker, Boey, and McDonald, 2003; Lavelle and Scully, 2005; Parkin and Bray, et al., 2005) making it the 12th most common malignancy. About 300,000 cases will arise in males, 33% of them affecting the pharynx, and 130,000 cases in females, 20% of them affecting the pharynx. Men are more than twice as often affected as women. There is no consensus as to which sites ought to be included in epidemiological surveys of oral cancer (Walker, Boey, and McDonald, 2003). Oral cancer customarily includes sites such as lips, salivary glands, tongue, oral cavity and pharynx (Scully and Bedi, 2000; Finnish Cancer Registry, 2003; Walker, Boey, and McDonald, 2003). The incidence of oral cancer shows variability between countries and geographical regions. About two-thirds of new oral cancer cases arise in developing areas, such as Africa, Central and South America, the Caribbean, China, parts of Asia, Melanesia, and Micronesia/Polynesia (Scully and Bedi, 2000; Walker, Boey, and McDonald, 2003; Parkin, 2004). In Finland, over 350 new oral cavity and pharyngeal cancers were detected in 2003, but according to incidence, these cancers are not included in the most common cancers (Finnish Cancer Registry, 2003). From the perspective of the 12 countries included in Northern Europe, the incidence of oral cavity and pharyngeal cancer in Finland ranks 10th in males and 3rd in females (Pukkala, and Söderman, et al., 2001).

It has been estimated that more than 75% of all oral cancers could have been prevented by refraining from smoking and alcohol abuse. Smoking or consumption of smokeless tobacco and excess of alcohol act synergistically and are the major risk factors for oral and pharyngeal cancers (Walker, Boey, and McDonald, 2003; Warnakulasuriya, Sutherland, and Scully, 2005; Syrjanen, 2005). Diet containing as-of-yet formally unidentified micronutrients of fresh fruits and vegetables is linked to a decreased risk of oral cancer (De Stefani and Deneo-Pellegrini, et al., 1999; De Stefani and Ronco, et al., 1999; De Stefani and Oreggia, et al., 2000; Walker, Boey, and McDonald, 2003; Rodriguez and Altieri, et al., 2004). Human papilloma viruses and herpex simplex virus may be associated with a proportion of oral and pharyngeal cancers (Walker, Boey, and McDonald, 2003; Syrjanen, 2005). Clinical entities, such as hyperplastic candidosis, tertiary syphilis, and immune deficiency, e.g., in HIV-infected individuals (not an independent risk factor for intraoral SCC), and familial genetic/non-genetic factors may predispose to oral cancer (Walker, Boey, and McDonald, 2003; Syrjanen, 2005).

Multistep and multifocal molecular level mechanisms underlie oral carcinogenesis. Understanding of such processes has provided targets for intervention in the reduction or the control of the prevalence of oral SCC and potential malignancies. These targets include protein kinase G, activator protein-1, nuclear factor-κB, signal transducer and activator of transcriptions, p53, demethylating agents, histone deacetylace inhibitors, antisense (downregulation of the expression of genes that stimulate tumor growth) and apoptosis-inducing molecules. Prospective randomized controlled trials will show the applicability of genetic and other alternative therapeutic modalities (e.g., gene therapy, retinoids, cyclo-oxygenase-2 inhibitors) on the screening, delay, arrest, and reverse of the oral carcinogenesis. (Chen, Fribley, and Wang, 2002; Johnstone, Ruefli, and Lowe, 2002; Sabichi and Demierre, et al., 2003; Xi and Grandis, 2003; Lavelle and Scully, 2005).

2.2 Surgical anatomy of the oral cavity and pharynx



Picture 1. Surgical anatomy of the oral cavity and pharynx.

The oral cavity (OC) is defined (Bailey, 2001) as the region that includes the lip mucosa, the cheek mucosa, the upper and lower alveolar ridges, the retromolar trigone, the anterior two thirds of the tongue, the floor of the mouth, and the hard palate. The oropharynx (OP) extends (Bailey, 2001) from an imaginary horizontal plane through the hard palate to another through the hyoid bone. Anteriorly, it opens to the oral cavity and includes the base of the tongue, the vallecula, the tonsillar regions, the posterior oropharyngeal wall, and the soft palate. The hypopharynx (HP) extends (Bailey, 2001) from the level of the hyoid bone to the inferior border of the cricoid cartilage. It includes the piriform fossa, the postcricoid region, and the posterior hypopharyngeal wall (Picture 1).

2.3 Current treatment options in oral and pharyngeal cancer

Patients with oral or pharyngeal SCC are treated widely by surgery and/or RT, which are the only curative treatments for carcinoma arising in the H&N. In the adjuvant setting, chemotherapy (CT) is useful but used alone, it is not curative (Mendenhall, Riggs Jr, and Cassisi, 2005; Scully and Porter, 2000). The staging system for cancer classification (TNM) (Sobin and Wittekind, 2002) is used for prognostication and choice of the treatment modality. The treatment strategy of an oral cavity or pharyngeal cancer patient is largely institutionally based (Parsons and Mendenhall, et al., 2002; Cosmidis and Rame, et al., 2004; Osborne and Brown, 2004; Andry, Hamoir, and Leemans, 2005; Ichimiya and Fuwa, et al., 2005; Klug and Wutzl, et al., 2005a; Klug and Wutzl, et al., 2005b). An interdisciplinary H&N tumor board including surgeons, oncologists, and other specialists, usually has a consensus treatment policy to offer the best outcomes (Scully and Porter, 2000).

Radiotherapy

RT can be administered on an outpatient basis without general anesthesia. RT has become more sophisticated with a decline in its side effects, as determined by several factors. These include total radiation dose, fraction size, radiated volume, fraction interval, treatment techniques, use of intensity-modulated RT as well as tissue-dose compensation, site and size of the primary tumor, and smoking habits during and after RT (Scully and Porter, 2000; Mittal and Pauloski, et al., 2003). Oral complications such as mucositis, decline of saliva volume and changes in saliva composition, oral and soft tissue pain, infection, loss of taste, and shooting toothache may manifest acutely during RT (Logemann and Smith, et al., 2001; Chambers and Garden, et al., 2004). Further, late complications of RT inducing chronic tissue degeneration include dental caries, soft tissue fibrosis, atrophy and necrosis, and osteoradionecrosis. These phenomena may hamper the patient recovery after several years (Scully and Porter, 2000; Logemann and Pauloski, et al., 2003; Chambers and Garden, et al., 2004). For RT-resistant tumors, and for salvage/failures after RT, surgery is available.

Surgery

In contrast to RT, surgery allows resection of the tumor and lymphatic tissue, and eventual reconstruction in a single-stage procedure. The surgical specimen is histologically examined. Healthy and clear tumor margins, ideally at least a 2 cm of clinically normal tissue, remains indispensable in multimodality treatment strategies involving surgery (Scully and Porter, 2000; Kovacs, 2004). To ensure cancer cure with minimum damage to healthy structures, the extent of the required neck dissection and the need for RT is determined by the tumor size and the nodal status of the neck (Parsons and Mendenhall, et al., 2002; Roy and Tibesar, et al., 2002; Doweck and Robbins, et al., 2003; Klug and Wutzl, et al., 2005b). Sentinel node biopsy may be useful in selected N0 cases to reduce the number of elective neck dissection and morbidity (Kovacs and Landes, et al., 2005; Nieuwenhuis and van der Waal, et al., 2005). Morbidity (infection, rupture of the carotid artery, salivary fistulae, chylorrhoea) and mortality are the disadvantages of surgery (Scully and Porter, 2000; Parsons and Mendenhall, et al., 2002).

The options for the reconstruction are the same for all tissue defects inside the oral cavity, from the lip to the pharynx. These techniques, from the least to the most laborious, include healing by secondary intention, direct closure, skin grafting, the use of local and regional flaps, and microvascular free tissue transfer (Neligan, Gullane, and Gilbert, 2003). Successful intraoral reconstruction necessitates not only management of all surgical techniques but comprehensive knowledge of the complex function of the UADT, the contribution of each site on the function, and the effect of resection and reconstruction on the function. When planning the reconstructive procedure, the patient's general medical condition, prognosis, history of previous RT, or upcoming RT, need to be considered (Neligan, Gullane, and Gilbert, 2003).

Free tissue transfers

Since their introduction over two decades ago, microvascular free tissue transfers have been used for intraoral reconstruction (Yang, Chan, and Gau, 1981; Muhlbauer, Herndl, and Stock, 1982; Song and Gao, et al., 1982). Free flaps are now considered the repair material of choice for most large defects (Neligan, Gullane, and Gilbert, 2003). Versatility, diversity, and safety of free flaps have made them particularly popular. Free flaps can be harvested from various sites. Any tissue type — skin, fascia, mucosa, muscle, tendon, bone or nerve — can be incorporated in the flap. Rich vascularity within the flap promotes rapid and secure healing. Despite the number of donor sites available, the free radial forearm flap, and the fibular osseocutaneous flap are, as of now, the most favorable flaps (Scully and Porter, 2000; Moerman and Vermeersch, et al., 2003; Neligan, Gullane, and Gilbert, 2003; Nicoletti and Soutar, et al., 2004a; Nicoletti and Soutar, et al., 2004b; Borggreven and Verdonck-de Leeuw, et al., 2005) for the reconstruction of the oral cavity, mandible, and pharynx.

2.4 Postoperative outcome after free tissue transfer in oral and pharyngeal cancer

The traditional outcome parameters after cancer treatment include overall survival (OS), disease-free survival (DFS), disease-specific survival (DSS), and treatment-related complications. After treatment, however, the functional result is of utmost importance for the quality of life (QOL) of the patient. Modern surgery aims at the greatest maintenance of function. Recent outcomes after surgical treatment with/without RT or CT of comparable studies of oral cancer in terms of OS, DFS, DSS, complications, QOL, and the functional outcomes in terms of speech, swallowing, and sensation, are reviewed separately each under the appropriate heading.

Survival

Many studies refer to high, unimproved overall mortality rates for intraoral SCC. This implies that the 5-year OS has been less than 50% for the past several decades (Gleich and Collins, et al., 2003; Walker, Boey, and McDonald, 2003; Wolff, Hassfeld, and Hofele, 2004). Improved accuracy in tumor staging, tumor imaging, and in surgical, RT and CT techniques may, however, have led to improved survival. This is supported, for example, by a large single-institution study on over 3,000 SCC patients treated over four decades (Carvalho and Ikeda, et al., 2004).

Survival rate for SCC varies by tumor site and stage. These tumor parameters vary greatly from one study to another. Table 1 presents the comparable and contemporary survival outcomes for patient populations with principally advanced oral SCC (Marks and Lolachi, et al., 1996; Gleich and Collins, et al., 2003; Langendijk and de Jong, et al., 2003; Bova, Cheung, and Coman, 2004; Hinerman and Mendenhall, et al., 2004; Lin, Hsiao, and Tsai, 2004; Malone and Stephens, et al., 2004; Wolff, Hassfeld, and Hofele, 2004; Borggreven and Kuik, et al., 2005; Dinshaw and Agarwal, et al., 2005; Klug and Wutzl, et al., 2005b; Kovacs and Mose, et al., 2005; Ruggeri and Carlini, et al., 2005; Scharpf and Esclamado, 2005; Umeda and Komatsubara, et al., 2005). Not all patients received a free flap. The survival figures in the referred studies have been calculated by the Kaplan-Meier method. For OS, all patients in the study were included. Disease-specific survival (DSS) refers to the patients who died of cancer recurrences and metastases. Subjects who died from some other cause are excluded. Disease-free survival (DFS) means the length of time after treatment during which no disease is found.

Complications

Microvascular flaps are safe in the reconstruction of an oral oncologic defect in terms of high flap survival rate and low mortality (95% and 4%, respectively, in the selected studies) (Table 2) (Simpson and Murphy, et al., 1996; Shaari and

Buchbinder, et al., 1998; Ryan and Hochman, 2000; Beausang and Ang, et al., 2003; Eckardt and Fokas, 2003; Chepeha and Annich, et al., 2004; Nakamizo, Yokoshima, and Yagi, 2004; Ross and Hundal, et al., 2004). Despite this success, a considerable amount of postoperative surgical and medical complications occur among patients, lengthening the hospital stay (Beausang and Ang, et al., 2003). The complications are related to the compromised general health of the oral cancer patients, their medications, tobacco and alcohol use, their advanced age, and the length of operation time (Simpson and Murphy, et al., 1996; Shaari and Buchbinder, et al., 1998; Beausang and Ang, et al., 2003; Eckardt and Fokas, 2003). Of the parameters in Table 2, flap survival, perioperative mortality, reoperation and fistula rate are rather unequivocally defined in the studies referred. The surgical, medical, or general complications encompass a greater amount of inconsistency. Partial flap necrosis, for example, was not regarded as a complication when not requiring any treatment (Chepeha and Annich, et al., 2004). In another study, however, partial flap necrosis represented a minor surgical complication (Ryan and Hochman, 2000). Generally, major surgical problems were managed in an operation theatre, and major medical problems were life threatening.

Table 1. **Survival (Kaplan-Meier) after surgery with or without RT and/or CT in oral and pharyngeal SCC.**

Study	No. of patients	Tumor site	Tumor stage	Surgical procedure	DSS	1-year OS or DFS (%)	2-year OS or DFS (%)	3-year OS or DFS (%)	5-year OS or DFS (%)
Borggreven 2005	100	oral/oro-pharyngeal	II/IV	FF[1]-repair					62 (OS)
Dinshaw 2005	348	H&N[2]	I/IV	NA[3]					56 (DFS)
Klug 2005	222	oral cavity/ oropharynx	II-IV	FF pre-dominantly	70.0 (5-year)		76.2 (OS)		62.4 (OS)
Kovacs 2005	94	oral cavity/-oropharynx	I/IV	NA					80 (OS)
Ruggeri 2005	33	oral cavity	III/IV	NA					54.5 (OS)
Scharpf 2005	28	hypo-pharynx	III/IV/recurrent	FF-repair					48.5 (OS)[4]
Umeda 2005	71	tongue	I/II	NA					93.8-95.4 (OS)
Bova[5] 2004	20	tongue	IV/recurrent	FF included	38 (5-year)				34 (DFS)
Hinerman 2004	226	oral cavity	I/IV	NA	67				47 (OS)
Lin 2004	78	oral cavity	II/IV/recurrent	FF included				38-70 (OS)	38-64 (OS)

Malone 2004	40	tongue base	III/IV	no FF	93.6 (2-year)		74.7 (OS)		
Wolff 2004	136	oral cavity; inferior parts	I/IV	FF included					57-70 (OS)
Gleich 2003	363	H&N[6]	III/IV	NA	60 (5-year)	NA	55 (OS)	46 (OS)	38 (OS)
Langendijk 2003	217	oral cavity	I/IV	NA				50-74 (OS)	
Marks 1996	38	pyriform sinus	I/IV	NA					34.6 (DSF)

[1] Abbreviation: FF, free flap.
[2] OC, HP, larynx, OP.
[3] Abbreviation: NA, not applicable.
[4] 4-year survival.
[5] 1 patient presented with adenocarcinoma vs. SCC.
[6] OP, OC, larynx, HP, sinus.

Review of the literature

Table 2. Complications after free flap surgery in H&N cancer.

Study	No. of patients	Mean/median age (y)	History of RT (%)	Flap survival (%)	Perioperative mortality[1] (%)	Reoperation rate (%)
Simpson 1996[3]	150	51(♂) 57,5(♀)	38	95	4.7	20
Shaari	52	74	41	100	6	6
1998[4]	35	55	44	94	0	9
Ryan 2000[5]	97	NA	18	91	1	NA
Beausang 2003[6]	288	NA	NA	94	0.3	10
Eckardt 2003[7]	479	52.5	NA	94	3.1	8
Chepeha 2004[8]	71	58	52 preop 38 postop	97	0	NA
Nakamizo 2004[9]	182	60.9	NA	97.3	0.5	3.7
Ross	57[10]	6-87(range)	100	93	10	NA
2004	63[11]	23-78 (range)	0	97	0	NA

[1] Death within 30 days of the operation.

[2] Abbreviation: NA, not applicable.

[3] 128 (85%) flap reconstructions for malignancy. Location of 85% of the lesions: intraoral soft tissues, laryngopharynx or mandible.

[4] A review of complications for pts > or < 70 years. Of the lesions, 80-89% in the OC, OP or HP.

[5] 92% of the pts had a malignancy. Of the cases, 67% were reconstructed for an OC/mandible, glossectomy or pharyngeal defects.

[6] All pts had an intraoral malignancy.

[7] 92% of the pts were operated on because of H&N cancer. Of the lesions, 84.3% were in the OC, OP or mandible.

[8] 91% of the pts underwent 1st or 2nd extirpation in the OC, OP or HP. Of the lesions, 79% were SCC.

[9] All lesions malignant, 76% of which were located in the HP, OC or OP.

[10] Recurrent H&N cancer. 89.5% were SCC. Of the lesions, 86% were in the OC or OP. All pts received intraoperative brachytherapy.

[11] Primary H&N cancer. 92% were SCC. Of the lesions, 92% were in the OC, OP or HP. No brachytherapy included.

Table 2. Complications after free flap surgery in H&N cancer (cont.)

Fistula rate (%)	Major surgical (%)	Minor surgical (%)	Major medical (%)	Minor medical (%)
NA[2]	23 (major and minor)		67 (major and minor)	
2	13	24	4	7
3	23	34	0	6
3	26	7	14	6
NA	NA	20	12 (major and minor)	
NA	NA	NA	NA	NA
5	8 (major surgical/medical) 21 (minor surgical/medical)			
NA	NA	NA	NA	NA
12	38 (wound complication)		83.3 (incidence of general complication)	
2	16 (wound complication)		52.4 (incidence of general complication)	

Quality of life

Quality of life (QOL) is an important outcome measure in health care practice and research, especially in oncology. QOL evaluation as a technique of clinical research has been increasingly used from the beginning of the 1970's (Editorial, 1996; Testa and Simonson, 1996). QOL has now reached the position of a new heading in books and medical journals. *Quality of Life Research*, for example, had and impact factor of 1.820 in 2004.

QOL, or more specifically, health-related QOL, refers to the measurement of disparity between the perceived observable well-being of an individual in the physical, psychological, functional, and social components (domains), and one's ideal health (D'Antonio and Zimmerman, et al., 1996; Testa and Simonson, 1996; Schwartz, Patrick, and Yueh, 2001). QOL is both a subjective and a dynamic phenomenon (Long and D'Antonio, et al., 1996; Allison and Locker, et al., 1998). An adequate QOL scale covers each subjective and objective components important to the population (coverage), gives consistent values in repeated measurements (reliability), measures what it claims to measure (validity), provides a change in the observed score, which is highly associated with the change in QOL (responsiveness), and is able to reflect true differences in QOL (sensitivity) (Testa and Simonson, 1996). Comprehensive QOL study often necessitates use of generic, or global, and disease-specific QOL instruments. These two contribute unique information about QOL (D'Antonio and Zimmerman, et al., 1996; Bjordal, 2004; Ren and Kazis, et al., 2005). A global instrument measures a wide range of domains and is not specific to any disease, health state, condition, or patient population (D'Antonio and Zimmerman, et al., 1996; Testa and Simonson, 1996). A disease-specific measure focuses on the domains most relevant to this disease.

Assessment of QOL is especially relevant to oral cancer patients. Surgery and RT often adversely affect facial harmony and such basic functions as breathing, speaking, chewing, and swallowing. Such deviating functions and appearance may be negatively perceived by others. Several validated questionnaires are available for UADT QOL study (D'Antonio and Zimmerman, et al., 1996; Hassan and Weymuller, 1993; Bjordal and de Graeff, et al., 2000; Weymuller and Yueh, et al., 2000a). The association between clinical and sociodemographic variables and QOL is inconsistent.

Hammerlid et al. (Hammerlid and Bjordal, et al., 2001), and Bjordal et al. (Bjordal and Ahlner-Elmqvist, et al., 2001) reported results of a prospective QOL study performed on 357 H&N cancer patients at baseline and during a 1-year follow-up. Of their patients, 59% had a tumor in the oral cavity and pharynx, 57% presented with stage III-IV disease, and 37% underwent surgery with or without adjuvant therapy. At baseline, the advanced stage showed a stronger association with low QOL than did age and sex. Hypo- and nasopharyngeal sites were more strongly related to worse QOL than other tumor locations. Women had more functional and emotional problems than males. During the one-year follow-up, tumor stage and site continued to be statistically and clinically significant factors predicting QOL. Patients with pharyngeal tumors scored worst. The impact of treatment type on QOL was not studied. The same patient population was assessed yet in another study for mental distress and psychiatric morbidity (Hammerlid and Ahlner-Elmqvist, et al., 1999) during a 1-year follow-up period. About one-third of the patients at each follow-up point were suspected to suffer from a major mood disorder.

In a cross-sectional study by Allison et al. (Allison and Locker, et al., 1998) on 188 UADT cancer patients, global QOL was analyzed using the EORTC QLQ-C30. Of the cases, 70% comprised oral and pharyngeal patients, 49% had stage III-IV disease, and 67% received surgery with or without adjuvant treatment. The variables with the strongest predictive value of QOL were sociodemographic. Unemployment, older age, and female gender referred to a poor QOL score. Clinical variables with a weaker but significant predictive effect for QOL were the dental status, cancer stage and cancer site. Edentate patients and those diagnosed with lower stage oral disease, as opposed to fully or partly dentate, higher stage pharyngeal or laryngeal patients, showed good QOL. The best 3 predictors of poor global QOL among the domains were emotional, breathing, and physical problems. Cancer treatment modality showed no impact on QOL.

Morton (Morton, 2003) examined 201 patients from two cultures, of whom 76% had oral, oropharyngeal, or hypopharyngeal cancers, 62% had stage III-IV, and more than 50% underwent surgery and RT. Sex and tumor stage had no impact on QOL after therapy. Supraglottic and hypopharyngeal tumor sites referred to the lowest QOL scores at the beginning of the follow-up, but the differences attenuated later. Combined treatment and neck dissection added problems. Global QOL improved over time. Experience of psychological stress and head and neck pain was significantly different depending on the cultural background of the participant.

Rogers et al. (Rogers and Lowe, et al., 2002) examined clinical function and QOL in a follow-up study of 130 oral cavity and oropharyngeal SCC patients. Of them, 45% had an advanced tumor (T3-4), 81% received a microvascular free flap, and 48% required adjuvant RT. According to their results, smaller tumor size, higher clinical functional score, and a less demanding type of operation were the main predictors of good QOL. The functional deficits at baseline persisted during the follow-up. Patients with better function had better QOL irrespective of tumor size or operation type. Here, tumor site, patient age and sex did not impact QOL.

Speech

Speech, among other oral functions, has been recognized as highly important for good short and long term QOL after oral cancer treatment (Colangelo and Logemann, et al., 1999b; Rogers and Laher, et al., 2002; Rogers and Lowe, et al., 2002; Vartanian and Carvalho, et al., 2004). The entire vocal tract from the glottis to the lips creates vocal characteristics that make the speaker identifiable to the listener. Complex somatosensory and motor systems delicately control and regulate speech. Expiratory airflow is converted into voice in the larynx. Subglottal pressure serves as the energy pump in speech production. Subglottal pressure tends to be kept regulated by precise control over the movement of the upper airway constriction-forming structures, i.e., glottis, velopharynx, tongue, mandible, alveolar ridge, teeth, lips and nose (Warren, 1986). The further refinement of phonation into speech sounds is mediated by the movements of the speech articulators. The major articulator is the tongue. Most speech sounds are produced by altering the shape of the tongue. Despite substantial adjustability of speech articulators and respiratory effort in optimizing speech performance, treatment of cancer in the oral cavity and oropharynx often results in impaired speech (Borggreven and Verdonck-de Leeuw, et al., 2005; Bressmann and Sader, et al., 2004; Hara and Gellrich, et al., 2003a; Hsiao, Leu, and Lin, 2002; Mady and Sader, et al., 2003; McCombe and Lyons, et al., 2005; McConnel and Pauloski, et al., 1998; Moerman and Vermeersch, et al., 2003; Nicoletti and Soutar, et al., 2004b; Pauloski and Logemann, et al., 1998; Seikaly and Rieger, et al., 2003; Yoshioka and Ozawa, et al., 2004; Zimmermann and Sader, et al., 2003). In fact, speech may already have been hampered by the presence of the tumor inside the mouth (Borggreven and Verdonck-de Leeuw, et al., 2005; McKinstry and Perry, 2003).

Balanced speech aerodynamics are necessary for a proper speech outcome (Warren, 1986; Laine and Warren, et al., 1988; Warren, Dalston, and Mayo, 1994; Hinton and Warren, 1995). Impaired velopharyngeal (VP) function leads to increased or excessive nasal resonance — hypernasality — that is heard on vowels and the sonorant consonants of a language. VP insufficiency may emerge as audible nasal emission or turbulence of air accompanied or co-produced by distorted plosives (e.g., /k/, /p/, and /t/) reducing speech acceptability and intelligibility (Warren, 1986; Warren, Dalston, and Dalston, 1990; Haapanen, 1991; Warren, Dalston, and Mayo, 1994). Compensation of VP insufficiency by misarticulation may further debilitate speech intelligibility (Warren, 1986). Because speech intelligibility and social acceptability are highly impacted by VP closure, its role is emphasized in craniofacial research although other laryngeal, pharyngeal and oral architecture similarly influence speech quality.

Seikaly et al. presented aeromechanic, acoustic and perceptual data on the VP function of 18 OP patients who had undergone resection of primary cancer and reconstruction with RFFF with or without RT (Seikaly and Rieger, et al., 2003). Their results indicated that speech intelligibility and the amount of the palate or tongue base resected were not significantly related. Resections of half or more of the soft palate led to significantly higher VP orifice areas and nasalance values, but not to a significant reduction in speech intelligibility. Likewise, the effect of RT on the measurements was found to be insignificant.

Nicoletti et al. instrumentally analyzed the increase of noise in voiceless fricative segments, /s/, /sh/, /f/, and /th/, and the patient himself or herself and a listener rated speech intelligibility. A total of 196 patients who had undergone surgery for oral cancer affecting sites from the anterior floor of mouth to the retromolar trigone were assessed (Nicoletti and Soutar, et al., 2004b). Of these patients, 43% received RFFF, and 16% another type of free flap reconstruction. RT was part of the treatment whenever necessary. These researchers pointed out two key anatomical sites for a good functional outcome. The first site was the midline anterior floor of the mouth, where resections that caused loss of integrity of the genioglossus and geniohyoid muscles severely impaired articulation. In unilateral resections, the intact contralateral side seemed to provide support for adequate function. The second key anatomical site was the soft palate. All resections led to a remarkable deterioration of speech, always attributable with hypernasality, although this did not affect pure articulation. All measures of speech quality showed better functional outcome with smaller excisions in the areas affecting the tongue. In all, the overall speech quality was related to the extent of surgical destruction, but not to the reconstruction modalities. RT worsened speech outcomes.

In another study, by Borggreven et al. (Borggreven and Verdonck-de Leeuw, et al., 2005), speech was examined in terms of communicative suitability and intelligibility by rating perceived nasality, articulation and consonant errors. The 76 patients analyzed presented with tumors in the OC and OP. All patients were reconstructed with RFFF and received RT whenever indicated. The postoperative overall speech outcome deviated significantly from that before the operation. Tumor size significantly affected articulation, whereas tumor site did not. Patients with tonsil or soft palate tumors were significantly more often hypernasal. The voice resonance was most sound in the patients with a tumor in the floor of the mouth. Consonant errors were significantly related to tumor size and site, meaning better results for smaller tumors and for tumors in the base of the tongue. The tonsil was the tumor site with most consonant errors. Intelligibility was more clearly related to articulation than to nasality. With respect to correct pronunciation of the target consonants, /k/, /s/, /d/, and /t/ proved the most difficult, with /k/ being the most abnormal. The effect of RT was not analyzed.

Hara et al. compared the effect of the flap type in OC and OP cancer patients. Smaller defects were reconstructed with RFFF (n = 7), and lateral upper arm free flap (LUFF) (n = 18) was used after large resections (Hara and Gellrich, et al., 2003a). They concluded that speech outcome in terms of monosyllabic word intelligibility deteriorated postoperatively with no significant effect of the flap type or tumor site. Tumor size was not analyzed.

McCombe et al. evaluated 8 patients who had undergone major soft palate resection, due to SCC, and reconstruction with RFFF, with or without RT (McCombe and Lyons, et al., 2005). The mean speech function was found to be obviously abnormal and requiring some repetition. Significant impairment was detected in palatal function and speech intelligibility. Partial palatectomy compensated by movements of the soft palate remnants and intact OP walls provided the best function, whereas palate motion was very limited in patients with defects in more than 75% of the palate.

Hsiao et al. compared the speech outcomes of 6 patients having undergone hemiglossectomy with primary defect closure to another 6 patients with RFFF reconstruction after hemiglossectomy (Hsiao, Leu, and Lin, 2002). The surgical defect included the mobile tongue and tongue base. Speech was measured by maximum syllable repetition rate, multiple rhyme test, and assessment of intelligibility, articulation, and types of errors. Patients with primary closure scored higher intelligibility and articulation ratings than those with flap reconstruction. Misarticulations with fricatives and affricatives were shown by all flap reconstructed patients. Several of them experienced problems also with laterals and plosives. Primary closure patients presented with fewer misarticulations with fricatives and affricatives, and none with laterals and plosives. The difference in the syllable repetition rate between the groups was insignificant. The effect of RT was not analyzed.

McConnel et al. conducted a comparison between primary closure, distal flap and free flap reconstruction after surgery for small OC or OP cancer (McConnel and Pauloski, et al., 1998). Three sets of matched patient pairs were analyzed. Nine patients received a free flap. The methods used were conversational speech intelligibility and a sentence-articulation test to identify correct and incorrect consonant articulation. The patients with primary closure had significantly higher conversational intelligibility than did patients with distal flap reconstruction, whereas difference in the consonant errors between the groups was insignificant. Primary closure vs. free flap groups and distal flap vs. free flap groups did not differ significantly from each other with respect to the speech outcome measures. Primary closure resulted in the best speech outcome. Distal or free flaps proved no superiority over each other in relation to speech.

Pauloski et al. examined surgical variables affecting postoperative speech after resection of OC or OP (Pauloski and Logemann, et al., 1998). Speech outcome measures for the 142 patients included the percentage of conversational understandability, the percentage of correct consonant phonemes, and a standard articulation test. Twenty-six patients received a free flap and 28 a distal flap. The rest of the patients were operated on with no closure, with primary closure, or with a skin graft. Speech outcome measures were related to treatment parameters. Larger tissue resections were related to worse speech function. Conversational understandability and the percentage of correct consonants were associated with the extent of resection to the tongue, the floor of mouth and the soft palate, and with the total tissue volume resected, as well as the closure type. Those patients who underwent reconstruction with free or pedicled flaps were more likely to have worse speech function as compared to patients closed primarily or with a skin graft, even when the extent of resection was similar. The combination of the surgical variables of the reconstruction type, the percentage of oral tongue, and the percentage of soft palate excised were most strongly associated with overall speech function.

Bressmann et al. studied the relationship of tongue motility and consonant intelligibility in 14 partial glossectomy patients who had received a local closure or a closure with a platysma flap + RT (Bressmann and Sader, et al., 2004). Consonant intelligibility reduced moderately. Patients with an intact genioglossus muscle had a significantly better intelligibility score. Consonant intelligibility was moderately but significantly related to tongue motility. Consonant acceptability was even more strongly related to the tongue motility. This affirms the importance of good tongue motility. Place consonant errors and tongue motility were inversely and significantly correlated. The study supported use of thin platysma flaps after partial glossectomy.

Promising reports have been published of pharyngoplasty techniques in extended resections of the soft palate; these show improvement over the poor speech results often encountered with palatectomies (Moerman and Vermeersch, et al., 2003; Hashikawa and Tahara, et al., 2005).

Both the subjects and methods of assessment varied greatly in the referred speech studies. The speech tasks were instrumentally or perceptually analyzed. Speech was evaluated by the patients themselves, by single listeners, and by panels of listeners formed by naïve or linguistically highly trained evaluators. The functions tested were oral function and articulation of single phonemes, words or sentences, and speech intelligibility and acceptability. The communicative intelligibility was assessed from words without context or from longer text passages.

Swallowing

Swallowing and speech use the same structures in the multifaceted tube UADT. UADT oncological surgery often debilitates swallowing. Several H&N cancer researchers report swallowing and speech concurrently (McConnel and Pauloski, et al., 1998; Hsiao, Leu, and Lin, 2002; Mady and Sader, et al., 2003; Seikaly and Rieger, et al., 2003; McCombe and Lyons, et al., 2005). It is not evident, why many studies report worse results for swallowing than speech (Hsiao, Leu, and Lin, 2002; Mady and Sader, et al., 2003; Nicoletti and Soutar, et al., 2004a; McCombe and Lyons, et al., 2005). It has been suggested that postoperative adjustment strategies for swallowing are more difficult to find than for speech (Mady and Sader, et al., 2003). It is also possible that swallowing, because of its universal vitality, might rank higher in importance in the study protocols than speech (Deleyiannis, Weymuller, and Coltrera, 1997; Rogers and Laher, et al., 2002).

The swallowing apparatus is a configuration of bone and cartilage, striated muscles, nerves, and soft, moist tissues lining the spaces. For study purposes, swallowing is divided into four phases — preparatory, oral, pharyngeal, and esophageal. During the preparatory phase, the oral tongue distributes the food to be tasted, chewed, blended with saliva, and compiles food from around the mouth into a single, cohesive bolus. The oral phase implies the transportation of the bolus into the pharynx. Prior to the pharyngeal phase and the bolus squeezing from the pharynx into the esophagus, the VP port and the larynx must close and the upper esophageal sphincter open. The esophageal phase involves the bolus propulsion into the stomach. These events are under the control of various systematic mechanisms and are affected by the volume and viscosity of swallowed food. Normally, the entire swallowing sequence lasts 1 – 1.5 seconds and occurs spontaneously once a minute in an awake subject. Swallowing occurs highly automatically, efficiently and safely in a healthy undamaged UADT (Dodds, Logemann, and Stewart, 1990; Mittal and Pauloski, et al., 2003).

Prior to treatment, the tumor within UADT often interferes with the neuromuscular regulation of swallowing. Pauloski et al. and Stenson et al. detected that advancement in the tumor stage and infero-posterior shift of the tumor location were negatively associated with swallowing function (Pauloski and Rademaker, et al., 2000; Stenson and MacCracken, et al., 2000). Normal aging may already have attenuated the swallowing reserves of UADT cancer patients who are typically middle-aged and older (Logemann and Pauloski, et al., 2000; Logemann and Pauloski, et al., 2002). The cancer treatment, radical operations followed by reconstructions and RT in particular, may further impair swallowing. Nonsurgical organ-sparing protocols utilizing chemoradiation in UADT cancer have not yet reported a revolution in function-sparing (Lazarus and Logemann, et al., 2000; Smith and Kotz, et al., 2000; Kotz and Costello, et al., 2004).

In order to secure a cancer cure in the management of advanced UADT tumors, multimodality therapy typically involving surgery and RT is generally recommendable. The impact of surgery on swallowing is determined by the tumor stage, site, and range of resection (Logemann and Pauloski, et al., 1993; Pauloski and Logemann, et al., 1993; Hara and Gellrich, et al., 2003b; Mittal and Pauloski, et al., 2003; Nicoletti and Soutar, et al., 2004a; Pauloski and Rademaker, et al., 2004). However, the impact of the reconstruction type is not obvious (Logemann and Pauloski, et al., 1993; Pauloski and Logemann, et al., 1993; McConnel and Pauloski, et al., 1998; Hara and Gellrich, et al., 2003b; Mittal and Pauloski, et al., 2003; Nicoletti and Soutar, et al., 2004a; Seikaly and Rieger, et al., 2003; Skoner and Andersen, et al., 2003; Pauloski and Rademaker, et al., 2004). During the postoperative convalescence, the acute and late side effects of RT with or without chemotherapy often complicate swallowing (see chapter Radiotherapy) (Pauloski and Logemann, et al., 1993; Pauloski and Logemann, 2000; Logemann and Smith, et al., 2001; Pauloski and Rademaker, et al., 2002; Logemann and Pauloski, et al., 2003; Mittal and Pauloski, et al., 2003; Nicoletti and Soutar, et al., 2004a; Skoner and Andersen, et al., 2003; Chambers and Garden, et al., 2004).

Seikaly et al. (Seikaly and Rieger, et al., 2003) and Skoner et al. (Skoner and Bascom, et al., 2003) presented swallowing data for similar free flap reconstructed patients whose T1-4, stage III-IV cancers were defined into OP. Seikaly's patients received RT if necessary, whereas all Skoner's patients underwent a full course of RT. Six to 12 months after operation, in the study by Seikaly et al., 94% of the patients consumed a normal or soft diet, and 1 patient was on enteral nutrition. Aspiration was detected in 8/128 swallows (6%) during a modified barium swallow. Nasal reflux was detected in 7/18 patients. These investigators concluded, based on statistics, that the amounts of base of tongue and palate resected were not associated with the incidence of nasal reflux, or laryngeal penetration or aspiration. Skoner et al. reported swallowing results based on how patients tolerated oral intake. Within 4 months of surgery, 50% of patients consumed all nutrition orally, whereas 50% were gastrostomy-tube dependent.

Nicoletti et al. (Nicoletti and Soutar, et al., 2004a) studied 196 patients with tumors in the OC and OP, of whom 59% were reconstructed with free flaps. Of the participants, 64% received RT. Swallowing data was derived from the patients' self-questionnaire. This investigation discovered a significant correlation between the swallowing function and the size of resection. The reconstruction method and the swallow outcome showed no significant associations within the groups homogenous for site and size. RT debilitated swallowing in the general sample, which, however, may have been caused by confounding effect of the tumor size.

Hara et al. (Hara and Gellrich, et al., 2003a; Hara and Gellrich, et al., 2003b) assessed swallowing and tongue mobility with VFG in healthy controls, and for 22 patients with OC and pharyngeal cancers having undergone reconstruction with LUFF (n = 16) or RFFF (n = 7) with or without RT. Tongue mobility was significantly reduced irrespective of the flap type. Aspiration was present in 14% of the RFFF patients, and in 31% of the LUFF patients. The resection site was associated with the impairment of tongue mobility. Anterior resections as compared with middle or posterior resections caused the greatest debilitation in tongue mobility and swallowing.

Eight cancer patients having undergone resections of at least 50% of the soft palate and RFFF reconstruction with or without RT were investigated postoperatively by McCombe et al. (McCombe and Lyons, et al., 2005). Swallowing tests included a self-questionnaire, standardized swallowing tests, VFG, and nasoendoscopy. After operation, two patients needed gastrostomy tubes. The aspiration rate was not reported. Those patients with total or near total palatectomies had poor swallow efficiency, and gross VP insufficiency with liquid and paste.

Pauloski et al. (Pauloski and Rademaker, et al., 2004), McConnel et al. (McConnel and Pauloski, et al., 1998) and Hsiao et al. (Hsiao, Leu, and Lin, 2002) analyzed the effect of the reconstruction type on swallowing after cancer resection. In Pauloski's VFG study on 144 OC and OP patients, 40% received a free or a pedicled flap with or without RT, and the rest were closed either primarily or with a skin graft with or without RT. In the entire group, swallowing worsened as the resection volume in various sites increased. For patients reconstructed with flaps, the amount of tongue base resected correlated significantly with swallowing function, indicating fewer problems with smaller resections. The importance of the tongue base on swallowing was highlighted in a great many analyses (Pauloski and Rademaker, et al., 2004). The better the flap filled the resection volume, the better the swallowing function was detected. Those patients reconstructed with flaps had worse swallowing outcome than patients closed primarily or with skin grafts. RT was a significant negative prognosticator for swallowing. In Hsiao's bedside swallowing test, function was superior because of better tongue volume in the six patients having received an RFFF after hemiglossectomy compared to those six closed primarily after hemiglossectomy. Swallowing after relatively small OC or OP cancer resections was examined in McConnel's study with VFG. Also in this series, the tongue base showed its value for efficient swallowing. Primary closure as compared with closure with distal myocutaneus or free flaps resulted in better swallowing. No significant differences arose between distal or free flaps.

Sensation

Oral cancer therapy interferes negatively with intraoral sensation. Regardless of therapy, advanced age and smoking predict sensory deterioration (Aviv and Hecht, et al., 1992; Calhoun and Gibson, et al., 1992; Cordeiro and Schwartz, et al., 1997). Sensory loss is apparent after transecting sensory nerves (Bodin and Lind, et al., 1999). Furthermore, RT not only affects sensation acutely but also in a delayed fashion (Aviv and Hecht, et al., 1992; Santamaria and Wei, et al., 1999; Logemann and Smith, et al., 2001; Logemann and Pauloski, et al., 2003; Bodin Jaghagen, and Isberg, 2004; Chambers and Garden, et al., 2004). Intraoral sensory preservation or re-establishment has been believed to be important to UADT functions or QOL. Innervated free flaps were introduced for this purpose (Urken and Weinberg, et al., 1990).

After cancer surgery, sensation recovery has been observed in free flaps used to restore the mucosal lining of the OC or OP, both with and without nerve anastomosis (Urken, 1995; Vriens and Acosta, et al., 1996; Santamaria and Wei, et al., 1999; Urken, 2004). It is suggested that in noninnervated flaps, sensation recovery takes place through neural ingrowth from the peripheral mucosa and the bed in the recipient site (Vriens and Acosta, et al., 1996; Santamaria and Wei, et al., 1999; Urken, 2004). The exact mechanism underlying the sensation recovery in innervated flaps, however, is not known (Santamaria and Wei, et al., 1999; Urken, 2004). Evidence exists that through microsurgical nerve anastomosis sensory recovery is better and faster (Santamaria and Wei, et al., 1999). Selection of the recipient nerve, and the microneural suturing technique, may further contribute to the success in sensory restoration. According to Santamaria et al., the lingual or inferior alveolar nerves, which have more extensive representation in the sensory cerebral cortex, proved superior to the posterior auricular nerve, cervical plexus, or the hypoglossal nerve in the sensory tests. End-to-end vs. end-to-side anastomosis showed significantly greater reliability (Santamaria and Wei, et al., 1999).

Whether usage of innervated free flaps in intraoral reconstructions ameliorates UADT function remains totally undetermined. Besides, with regard to over 150 years of debate and experimental research, no consensus prevails as to sensory feedback in humans is imperative for airway protection once the swallowing sequence is initiated (Jafari and Prince, et al., 2003). In fact, Bastian et al. demonstrated that normal and healthy swallowing can occur spontaneously under complete anesthesia of UADT mucosa (Bastian and Riggs, 1999).

3 Aims of the study

In advanced oral cancer, the most up-to-date surgical reconstruction method, i.e, free tissue transfers, has brought about abundant research concerning perioperative surgical outcome. Data on functional outcomes, in contrast, are scarce. The few studies focus on a specialized piece of outcome but do not describe the entire postcancer experience. Limiting functional studies to examination of single items or using a gross study design predispose the results and their interpretation to the so-called cancellation effect. This means that improvement in one item leads to deterioration in the other, resulting in an insignificant summary product (Weymuller and Yueh, et al., 2000b; Rogers and Laher, et al., 2002). In order to extract comprehensive treatment outcomes, we designed a prospective follow-up study for a population of patients with large OC or OP cancer, by determinating their:

1. Survival (I, II),
2. Postoperative complications (I, II),
3. Quality of life (II),
4. Speech (III, V),
5. Swallowing (IV), and
6. Intraoral sensation (IV, V).

4 Patients and methods

4.1 Study design and patients

Retrospective study (I)

Before the prospective study, the recent clinical experience of the institution on postoncological oral free flap reconstructions was reviewed. Fifty consecutive cancer patients having received a free flap for OC, OP, or HP reconstruction between 1989 and 1995, were retrieved from the computerized records of the Department of Plastic Surgery at Helsinki University Central Hospital. The patient and tumor characteristics, survival and postoperative complications were retrospectively analyzed.

Prospective studies (II-V)

From June 1996 to May 1999, 44 consecutive OC, OP, and HP cancer patients were prospectively followed-up at Helsinki University Central Hospital. An interdisciplinary H&N tumor board had agreed to recommended cancer resection, a free flap transfer with or without adjuvant RT and CT, for each patient. The medical and sociodemographic data for these patients were gathered preoperatively (PREOP). Survival and postoperative complications were analyzed. The follow-up for survival ended in March 2002. Operative procedures were performed by the same team. Measurements for QOL, speech, swallowing, and intraoral sensation were carried out by the same examiners PREOP and at four time-points, 6 weeks (POST6wk), 3 months (POST3mo), 6 months (POST6mo), and 12 months (POST12mo) after operation.

Table 3 presents the sociodemographic and the tumor characteristics of the patient population. ISCED is an abbreviation for International Standard Classification of Education (ISCED, 1997). Eight patients (18%) presented with a tumor recurrence. Because these recurrences are not mentioned repeatedly in the columns of Neck node status and Stage, the total percentage is 82% in each column. HP patients (7%) were not included in the statistical comparisons. Not all patients could complete all study visits. Patient dropout occurred during the prospective follow-up period almost exclusively due to death or referral for terminal care.

Table 4 shows the details of the therapy.

Table 3. Sociodemografic and tumor characteristics of the patient population of studies II-V.

Sociodemographic characteristic		Number of patients (%)	Tumor characteristic		Number of patients (%)
Sex	Male	29 (66)	**Tumor site**	Oral cavity	28 (64)
	Female	15 (34)		Oral pharynx	13 (29)
Smoking	Smoker	31 (70)		Hypopharynx	3 (7)
	Nonsmoker	13 (30)	**Tumor histology**	SCC	40 (91)
Medical conditions preoperatively		21 (48)		adenoid cystic carcinoma	3 (7)
	Hypertension	7 (16)		adenomatous polymorphic carcinoma	1 (2)
	Coronary heart disease	5 (11)	**Tumor size**	T2	20 (46)
	Diabetes mellitus	4 (9)		T3	5 (11)
Alcohol usage	No greater than moderate	26 (59)		T4	11 (25)
	Heavy (> 5 standard units of alcohol/day)	18 (41)		Tumor recurrence (typically large/multifocal)	8 (18)
Education	Tertiary education (ISCED 5/6)	10 (23)	**Neck node status**	N0	17 (39)
	Upper secondary education (ISCED 3/4)	8 (18)		N1	6 (14)
	Basic education (ISCED 0-2)	26 (59)		N2	12 (27)
Employment status	Working full or part-time	19 (43)		N3	1 (2)
	Retired	17 (39)	**Stage**	II	10 (23)
	Unemployed	8 (18)		III	8 (18)
				IV	18 (41)

Table 4. Therapeutic details of the prospective study.

Characteristic		Number of patients (%)
Free flap type	Radial forearm	34 (77)
	Fibula	1 (2)
	Jejunum	1 (2)
	Latissimus dorsi	2 (5)
	Latissimus dorsi and scapula	4 (9)
	Scapula	1 (2)
	TRAM[1]	1 (2)
Flap innervation	Yes[2]	27 (61)
	No	17 (39)
Mandible procedure	Midline mandibulotomy	22 (50)
	Lateral mandibulotomy	2 (5)
	Partial mandibulectomy	4 (9)
	Hemimandibulectomy	4 (9)
	Intact mandible	12 (27)
Neck procedure	Unilateral neck dissection	33 (75)
	Bilateral neck dissection	7 (16)
	None	4 (9)
Radiotherapy	Before microvascular transfer	5 (11)
	After microvascular transfer	34 (77)
Concomitant chemotherapy		4 (9)

[1] Abbreviation TRAM: transversus abdominis musculocutaneous.

[2] The greater auricular nerve was the recipient nerve in 93% of the flap transfers.

4.2 Ethical considerations

In all prospective studies, written informed consent was obtained from each participant. The ethics committee at each participating department had approved the studies.

4.3 Patient measurements

All prospective measurements were accomplished separately from the routine follow-up visits to minimize the likelihood of patients dropping out of the study for causes other than death or a referral for terminal care. The treatment protocol included no routine speech or swallowing therapy.

Quality of life (II)

The instrument used for assessing QOL was a Finnish translation of the original version of the University of Washington Quality of Life Questionnaire (UWQOL) (Hassan and Weymuller, 1993) (Table 5). UWQOL is short, self-administered H&N cancer specific measure validated more than a decade ago. The patients were carefully instructed to fill out the questionnaire appropriately under the supervision of M.M.-L. They scored nine domains from 0 (the greatest dysfunction) to 100 (the best function). Each category contributed equally to the final score, and each subset had four or five possible item choices. The sum of the nine domains (maximum 900) was divided by nine to achieve the final or composite score between 0 and 100.

Speech (III, V)

Speech was analyzed perceptually (V) and nasalance was evaluated instrumentally (III). Instrumental analysis was performed to measure the basic speech physiology. These measurements included aeromechanic VP orifice area (VP0) estimation by pressure and flow measurement techniques (Warren and Dubois, 1964; Warren, 1979) and measurement of nasal acoustic energy during speech, i.e., nasalance (Dalston, Warren, and Dalston, 1991). VP0 closure was measured using the Perci PC (Microtronics Corporation, Chapel Hill, North Carolina, USA). VP function was classified normal for VP0 values 0.0 to 0.05 cm^2, borderline for values greater than 0.05 up to 0.20 cm^2, and inadequate for values greater than 0.20 cm^2 (Warren and Dubois, 1964; Warren, 1979; Andreassen, Smith, and Guyette, 1992; Zajac, 2000). To control the nasal airway aerodynamics on VP function, nasal cross-sectional area (Nasa0) and nasal airway resistance (Nasar) were also estimated by Perci PC.

Table 5. University of Washington Quality of Life Questionnaire (UWQOL) (Hassan and Weymuller, 1993).

Pain	I have no pain.
	There is mild pain not needing medication.
	I have moderate pain — requires regular medication (codeine or non-narcotic).
	I have severe pain controlled only by narcotics.
	I have severe pain not controlled by medication.
Disfigurement	There is no change in my appearance.
	The change in my appearance is minor.
	My appearance bothers me but I remain active.
	I feel significantly disfigured and limit my activities due to my appearance.
	I cannot be with people due to my appearance.
Activity	I am as active as I have ever been.
	There are times when I can't keep up my old pace, but not often.
	I am often tired and I have slowed down my activities although I still get out.
	I don't go out because I don't have the strength.
	I am usually in a bed or chair and don't leave home.
Recreation/	There are no limitations to recreation home and away from home.
entertainment	There are a few things I can't do but I still get out and enjoy life.
	There are many times when I wish I could get out more but I'm not up to it.
	There are severe limitations to what I can do, mostly I stay home and watch TV.
	I can't do anything enjoyable.
Employment	I work full time.
	I have a part-time but permanent job.
	I only have occasional employment.
	I am unemployed.
	I am retired (circle one below).
	Not related to cancer treatment.
	Due to cancer treatment.
Chewing	I can chew as well as ever.
	I can eat soft solids but cannot chew some foods.
	I cannot even chew soft solids.
Swallowing	I can swallow as well as ever.
	I cannot swallow certain solid foods.
	I can only swallow liquid food.
	I cannot swallow because it "goes down the wrong way" and chokes me.
Speech	
	My speech is the same as always.
	I have difficulty with saying some words but I can be understood over the phone.
	Only my family and friends can understand me.
	I cannot be understood.
Shoulder	I have no problem with my shoulder.
disability	My shoulder is stiff but it has not affected my activity or strength.
	Pain or weakness in my shoulder has caused me to change my work.
	I cannot work due to problems with my shoulder.

In adults, a Nasa0 of 0.40 cm^2 or larger was considered adequate (Warren and Hairfield, et al., 1987), whereas Nasar, in normal adults, ranged from 1.0 – 3.5 $cmH_2O/L/s$, with a mean of approximately 2.5 $cmH_2O/L/s$ (Warren, and Hinton, et al., 1987). Nasalance represents objective and specific acoustic substitution of perceived nasality (Hardin and Van Demark, et al., 1992; Dalston, Neiman, and Gonzalez-Landa, 1993). Nasalance was determined by the Nasometer (model 6200, Kay Elemetrics, Pine Brook, New Jersey, USA) using sentences loaded with voiceless plosive consonants (Plos), i.e. /k/, /p/, /t/ and /s/, or voiced i.e. sonorant consonants (Sonor), i.e. /v/, /l/, and /r/. The Finnish reference value for nasalance was 13.5% (SD 7.3), the values 22 – 29% were considered borderline, and values > 29% indicated audible hypernasality (Haapanen, 1991). The Finnish reference values for nasalance agree very well with the values obtained in cross-cultural studies for comparable utterances (Dalston and Neiman, et al., 1993).

Perceptual speech analysis (V) was performed by a trained listener (M.-L.H., a medical speech pathologist) from speech samples recorded on tape (Sony TCD-D7 DAT Recorder, high-sensitivity microphone placed at mouth level, 25 cm from the lips). The variables examined were the articulatory ability of the dentoalveolar sounds /r/ and /s/, voice quality, and voice resonance. Each patient read a set of 36 2-syllabic words with /r/ and /s/ positioned at the beginning, middle, and end of the word. The misarticulations of /r/ and /s/ were categorized into three classes from mildest to severest, i.e., distortions, substitutions, and omissions. Voice quality was determined as normal vs. distorted, and voice resonance as normal vs. hyper- or hyponasal. Of the 179 speech samples, 31 (17%) were analyzed together with another trained listener (E.I.). The interjudge agreement was 0.94 for misarticulations of both /r/ and /s/, and 0.95 for voice quality and resonance. Based on the high consistency of the interjudge agreement of the speech samples, one-judge assessment was considered adequate. The patients self-rated the intelligibility of their speech according to UWQOL (Hassan and Weymuller, 1993) (Table 5). This rating (Sp-UWQOL) was compared with respect to the articulatory ability of /r/ and /s/, the medical and sociodemographic variables (Tables 3 and 4), and intraoral sensation.

Swallowing (IV)

The swallowing sequence was examined with videofluorography (VFG). The VFG was accomplished with the patients seated, and was always begun with 3 ml water-soluble injection agent (Omnipaque® Amersham Health) given perorally to test the safety of swallowing. If feasible, the patients completed a modified barium swallow. The patient was administered a few milliliters of liquid barium, but was also permitted to ingest larger boluses if he/she thus claimed to swallow more easily. VFG was continued with thick barium, and finished with one quarter of a barium-coated standard shortbread cookie. Not all participants could swallow all bolus consistencies. VFG procedures were conducted and assessed by an experienced (20 years on VFG) H&N radiologist (L.E.), and reviewed by another experienced

(10 years on VFG) H&N radiologist (S.R.). The percentage of patients on potentially mouth-drying medication (mostly prescribed for hypertension and mood disturbances) was constant throughout the study. The effects of the medication, subjective mouth dryness, or saliva secretion on swallowing were not studied.

The radiologists analyzed in turn all 166 videotaped swallowing sequences in slow-motion frame-by-frame (¾-inch U-matic, 30 frames per second) according to the elaborate protocol (see Study IV, Table 3). The esophageal phase was omitted. A plain chest X-ray was taken one year after the operation to detect any changes related to chronic aspiration. The radiologists created a simple summary VFG report (VFGR) (normal, mildly impaired, moderately impaired, or severely impaired) based on the detailed VFG protocol on swallowing for each patient. The interjudge agreement for the VFGR was 0.78. The radiologists re-assessed all discrepant VFG protocol ratings, achieving a consensus that served in the statistical analysis. The patients' self-rated swallowing ability (Sw-UWQOL) (Hassan and Weymuller, 1993) (Table 5) was examined in relation to the VFGR, the medical and sociodemographic variables, and intraoral sensation. Both VFGR and SR were converted into a scale from 10 (normal swallowing / I can swallow as well as ever) to 0 (severely impaired swallowing / I cannot swallow because "it goes down the wrong way" and chokes me).

Sensation (IV, V)

A moving two-point discrimination described elsewhere (Aviv and Hecht, et al., 1992; Vriens and Acosta, et al., 1996) was the method used for examination of intraoral surface sensation. Four sites, the tongue tip, the right and left lateral dorsal tongue, and the anterior hard palate 1 cm behind the gingival ridge were the areas tested for 2, 6, 10, and 15 mm discrimination. The Disk-Criminator (Baltimore, MD) developed by Mackinnon and Dellon was modified by dividing the disc into triangles, the base of which contained two thin metal rods with smoothened ends, 2, 6, 10, and 15 mm apart, and the apex of which was held in a fine clamp. The tongue tip was defined as the distal 1 cm of the anterior tongue. The lateral dorsal tongue was defined by a region 1 cm medial to the lateral border of the tongue and 2 cm anterior to the circumvallate papillae. The anterior hard palate was defined as the 1 cm area behind the gingival ridge. One author (M.M.-L.) tested all patients. The task was introduced to the patient by placing first the device on the forearm, then on the tongue tip, followed by the right and left lateral dorsal tongue, and the anterior hard palate. The testing series began with the longest inter-rod distance alternating at random between the longest and shortest distances. The device was moved on the mucosa for 1 cm from proximal to distal in about 1 second, with just enough pressure to cause an indentation. Each inter-rod distance was tested three times. To have correctly rated a particular distance, at least 2 of the 3 trials had to be right. For statistical correlations, a sensation instrument was designed. Correct discrimination of each distance gave 3 points, incorrect discrimination 2 points, and no sensation was as-signed 1 point. These points were summed up into a scale from 48 (4 correct discrimination on 4 sites, 3 points x 4 x 4 = 48) for the best sensation, and 16 (4 tests with no sensation on 4 sites, 1 point x 4 x 4 = 16) for no sensation. This scale was transformed from 10 (best sensation) to zero (no sensation). The results of the sensation instrument correlated (Spearman's correlation) highly significantly ($p < 0.00001$) with the bare sum of correct discrimination at the different follow-up points. The sensation instrument was indispensable to reveal shifts between the classes "incorrect identification" and "no sensation" taking into account the qualitative change in sensation.

4.4 Statistical methods

Survival rates after free flap operation were calculated using the Kaplan–Meier method. All available data was used in follow-up studies II-V. Confounding factors were sought by calculating first the survival rates using the Kaplan–Meier product limit method. The log-rank test was used to find differences in survival. Finally, multivariate proportional hazards regression was used to establish the variables most predictive of survival. HP tumor patients ($n = 3$) were excluded from all comparisons in studies II-V. Stepwise logistic regression, Fisher's exact, or the $\chi 2$ tests were used to find risk factors for surgical adverse effects and poor survival (I), swallowing (IV) and speech (V) disturbances in relation to selected medical, sociodemographic, and surgical group variables. Differences in composite QOL scores as a function of time (II) were examined in patients ($n = 20$) with no missing data using Friedman two-way ANOVA. The Wilcoxon signed-rank test was used to detect the change in the pre and postoperative domain QOL scores (II), objective and subjective swallowing (II) and speech (V) data, and sensation (IV, V). The Mann-Whitney U or the Kruskal-Wallis test were performed to show the differences and changes in QOL scores (II), speech (III, V), swallowing (IV), and sensation (IV, V) data of patients grouped by selected medical, sociodemographic, or surgical variables (sex, age, tumor site, tumor size and stage, sensate vs. nonsensate flap, mandible split vs. intact mandible, no more than moderate drinking vs. heavy drinking, no smoking vs. smoking, and unemployed vs. retired or employed), and as a function of time. Spearman's correlation was used to show associations between aerodynamic and nasalance values (III), and between swallowing (IV) and speech ratings (V). McNemar's test was used to find differences in incidences of selected swallowing (IV) and speech (V) characteristics during the follow-up. Goodness-of-fit testing was used in comparisons between the study population and the general Finnish reference population (II).

The statistical analyses were performed using the statistical software package NCSS, versions 6.0, 2000, and 2004 (NCSS Statistical Software, Kaysville, Utah, USA). Probability values of < 0.05 were considered to indicate statistical significance.

5 Results and discussion

5.1 Free flaps in oral and pharyngeal cancer (I-V)

General aspects

In the present studies, altogether 94 patients having received a free flap reconstruction for oral cavity or pharyngeal cancer over a period of 10 years (between 1989 and 1998) were analyzed for survival and surgery related complications. Forty-four consecutive oral cavity and pharyngeal cancer patients reconstructed with a free flap were recruited over a period of 3.5 years and followed-up in a prospective manner for functional outcome during a period of 12 months, which is a sufficient time to study these patients. For the functional studies, 50 consecutive patients were originally enrolled, but six (12%) were excluded because the PREOP study visit proved impracticable in each case. Of the 44 patients, one participant refused to complete all but the PREOP and the 12-month functional examinations, other patients stayed duly in the program. Such compliance among H&N cancer patients can be considered excellent. Both the prospective and retrospective patient materials comprise consecutive series of a tertiary referral center serving an area of approximately 1.4 million people. This data has been examined and the conclusions drawn are supported by the statistics.

The current patient populations represented typical H&N cancer populations. The male/female ratio was 2:1. The mean age in the retrospective study (Study I) was 57 (range, 13 – 79) years, and in the prospective study (Study II) 56.2 (range, 38 – 80) years. This data also supported the commonly held beliefs regarding the sociodemographic characteristics peculiar to H&N cancer patients. The patients differed significantly from the Finnish population in general with respect to employment and educational status, and smoking and drinking habits. The percentages of stage III, IV, and recurrent tumors in the retrospective study and the prospective study were 88% and 77%, respectively. The histological diagnosis of the tumor in retrospective study and the prospective study was SCC in 44/50 (88%) and 40/44 (91%) cases, respectively. For comparison in similar recent populations, the conventional therapeutic outcome measures, i.e., rates for survival, flap success, and complication were reviewed (Tables 1, 2).

Survival (I, II)

In the retrospective study, the mean follow-up time was 2.6 years (range, 26 days – 9.2 years). The mean survival time after the microvascular procedure was 1.6 years. The rates for 3- and 5-year OS were 42% and 23%, respectively. Patients with an OP tumor had the best prognosis, and those presenting with a HP tumor, the poorest. Stage was the attribute most strongly predicting survival. In the prospective study, 12/44 patients, (27%) were alive and disease-free after the mean follow-up time of 2.1 years (range, 5 days - 5.2 years). The mean survival time after the microvascular procedure was 1.3 years. The 1-, 2- and 3-year OS rates were 68%, 45% (M.M.-L., unpublished result), and 32% (M.M.-L., unpublished result). The 1- and 2-year DFS rates were 43% and 32% (M.M.-L., unpublished results). In the prospective study, tumor location in the OC (vs. OP), smoking (vs. non-smoking), heavy drinking (vs. no more than moderate drinking), and unemployed (vs. employed or retired) predicted worse survival. The survival rates in the retrospective and prospective studies compare well with each other and with those reported by others (Table 1). In the prospective study, unemployment and heavy drinking were the factors most predictive of survival, increasing the risk of dying 4.4-fold, and 2.4-fold, respectively. It is acknowledged that survival figures for those unemployed or drinking heavily may be representatives of the study protocol. This issue requires further study. However, heavy drinking and unemployment are easily sought from the patient history before operation. With careful orientation into the general medical condition of patients with signs of risk behaviours and social displacement, and with early pre and postoperative rehabilitation and support for these patients, treatment outcome in terms of survival may be improved.

Complications (I, II)

Free flap reconstructions in H&N cancer surgery are considered as major surgical procedures. Surgery-related complications are frequently reported. Rates for flap survival, perioperative mortality, reoperation, and fistulas are presented in Fig. 1.

Study	Flap survival (%)	Perioperative mortality (%)	Reoperation rate (%)	Fistula rate (%)
I (n = 50)	96	2	20	10
II (n = 44)	98	11	7	2

Figure 1. Complication rates after microvascular transfer.

The overall postoperative complication rates in the retrospective and the prospective study were 58% and 66%, respectively. The present complication rates are in line with those reported previously (Table 2). In the prospective study, the number of the patients (11%) who died within 30 days postoperatively was rather high. All of these patients had a history of smoking and heavy drinking and had presented with signs of being under the influence of alcohol on at least one study visit during the follow-up period. A medicolegal autopsy performed on each patient referred occasionally to the contribution of chronic alcohol use to their deaths. Risk analysis was, however, not feasible because of too few patients, and because acute or chronic alcohol use, or alcohol withdrawal, were not consistently measured in this study.

Methodological aspects (II-V)

H&N cancer patients are prone to dropout in a longitudinal study (Colangelo and Logemann, et al., 1999a; Colangelo and Logemann, et al., 1999b; Rademaker and Vonesh, et al., 2003). In the present study, the contacts with the patients were carefully maintained. To reduce the bias caused by the missing data, all available data at all time points were used in the functional studies II-V. This strategy was selected because restricting the analyses to study completers, i.e., patients with no missing data, might have demonstrated an excessively optimistic impression of the clinical course of the functional outcome. If patients with poorer outcome drop out, the current type of analysis, however, could present a more favourable picture of the outcome than is actually true, especially at later follow-up points when patients still in the study would have better functions (Rademaker, and Vonesh, et al., 2003). Statistical methods have been developed to account for dropout in a way that the resulting time course of data could be illustratable in a manner as unbiased as possible (Rademaker and Vonesh, et al., 2003). Such statistics were not used.

The current patients acted as controls for themselves as function over time, the PREOP measurement being one reference value. There is body of knowledge that the presence of an untreated oral cancer may alter the voice and articulation (McKinstry and Perry, 2003), impair swallowing (Pauloski and Rademaker, et al., 2000; Stenson and MacCracken, et al., 2000), and cause pain and anxiety. Randomization of cancer patients into treatment and nontreatment goups was not, for ethical reasons, optional. The use of a control group, however, is often advocated. Problems may arise, though, in the selection of an adequate control population. The study goal was to demonstrate the oral function after large oral cancer reconstructed with microvascular flaps. In the present study, after voluminous resections, primary closure, skin grafts, or distal flaps were not alternatives for the reconstruction method. Age and sex matched healthy controls would probably differ from the oral cancer population in general. The sociodemographic findings in this study would indicate that the control population should, furthermore, be matched by employment and educational status, co-morbidities, and tobacco and alcohol use. Comparison between a sufficient number of individuals as a function of time was considered the most appropriate setting for the examination of a particular treatment method in patients with resections of variable sizes.

The reported results in the literature may also reflect different study protocols. The tumor site, size, and stage as well as the type of reconstruction vary from one study to another. The current tumors were staged according to international classifications, but resection and flap volumes, which may be important, were not measured. Furthermore, the clinical experience of an institution, its customary practices and resources, influence the protocols of reconstruction, RT, dental rehabilitation, speech and swallowing therapy, dietary consultation, and other support.

5.2 Quality of life (II)

The mean QOL score was significantly better ($p < 0.0001$) pre than postoperatively in the prospective study. This comparison was possible for patients with no missing data ($n = 20$). Their composite scores before surgery, and 6 weeks, 3, 6, and 12 months after surgery were 87.37, 75.32, 75.78, 76.86, and 77.41, respectively. No significant postoperative improvement was detected during the 1-year follow-up. Unemployment predicted a lower composite score. The composite score and the domain scores for all patients are presented in Table 6.

Table 6. Mean UWQOL[1] domain scores to 12 months in patients[2] with an oral cavity or oropharyngeal tumor.

Domain	PREOP	POST6wk	POST3mo	POST6mo	POST12mo
Pain	76.42	86.52(*[3])	81.25(NS[4])	85.00(NS)	89.14(**)
Disfigurement	96.17	78.18(***)	79.47(***)	81.11(***)	82.14(***)
Activity	88.33	79.47(**)	81.82(**)	83.61(NS)	92.14(NS)
Recreation/entertainment	93.25	80.24(**)	84.45(**)	85.56(**)	92.43(NS)
Employment	62.58	66.48(NS)	64.83(NS)	60.56(NS)	50.29(*)
Chewing	73.33	60.00(**)	57.89(**)	63.33(**)	66.00(*)
Swallowing	86.25	76.67(**)	74.52(**)	79.86(*)	83.93(NS)
Speech	95.31	80.52(***)	82.83(***)	81.25(***)	84.46(***)
Shoulder disability	97.08	78.59(***)	75.18(***)	73.26(***)	82.68(**)
Composite score	85.41	76.30	75.80	77.06	80.36

[1] Abbreviation UWQOL: University of Washington Quality of Life Questionnaire (Hassan and Weymuller, 1993).

[2] No. of pts: PREOP (n = 38), POST6wk (n = 31), POST3mo (n = 29), POST6mo (n = 23), POST12mo (n = 23).

[3] The differences between pre and postoperative domain scores were examined by the Wilcoxon signed-rank test. Significances of p values are presented in parentheses in four categories as follows: * < 0.05, ** < 0.01, *** < 0.001.

[4] Abbreviation NS: not significant.

Positive prognostic factors for QOL have been described in other reports (Long and D'Antonio, et al., 1996; Rogers and Lowe, et al., 1999; de Graeff and de Leeuw, et al., 2000; Morton, 2003), as laryngeal (vs. oral and OP) tumors, anterior (vs. posterior) OC tumors, lower (vs. high) stage tumors, and after single (vs. multimodality) therapy. In this study, QOL scores for OC and OP patients were similar (Fig. 2). The impact of tumor stage remained unclear. The impact of RT was not formally analyzed because it was administered for 88% of the patients. A negative influence, however, is suggested, which may have equalized surgical effects. Results from previous studies concerning age and sex have been inconsistent or suggested better QOL in younger individuals and in men (D'Antonio, et al., 1996; Allison and Locker, et al., 1998; Long and Rogers and Lowe, et al., 1999; de Graeff and de Leeuw, et al., 2000). Here, effects of age and sex were clear in the domains of employment, and disfigurement, indicating that older patients were more likely to be retired, and female patients were more dissatisfied with their posttreatment appearances. Evidence exists, that facial appearance is of major concern for free flap patients, and that this problem may be poorly understood and overlooked in clinical practice (Millsopp and Brandom, et al., 2005). The present data also showed that low education and unemployment negatively influence QOL, which runs in contrast with a previous report (Long and D'Antonio, et al., 1996).

QOL was currently measured by the Finnish translation of the original version of the UWQOL (Hassan and Weymuller, 1993). UWQOL has been widely applied for patient populations in the United States, and also internationally (Rogers and Lowe, et al., 1999; Vartanian and Carvalho, et al., 2004). The original English UWQOL and its Portuguese translation have been earlier used without validation in Britain and Brazil, respectively (Rogers and Lowe, et al., 1999; Vartanian and Carvalho, et al., 2004). Consequently, the Finnish translation was not considered necessary to undergo psychometrical validation for this study. Our study would have most apparently profited by combining the disease-specific UWQOL with a generic QOL measure because both kinds of instruments reveal unique aspects of QOL (D'Antonio and Zimmerman, et al., 1996; Bjordal, 2004; Ren and Kazis, et al., 2005).

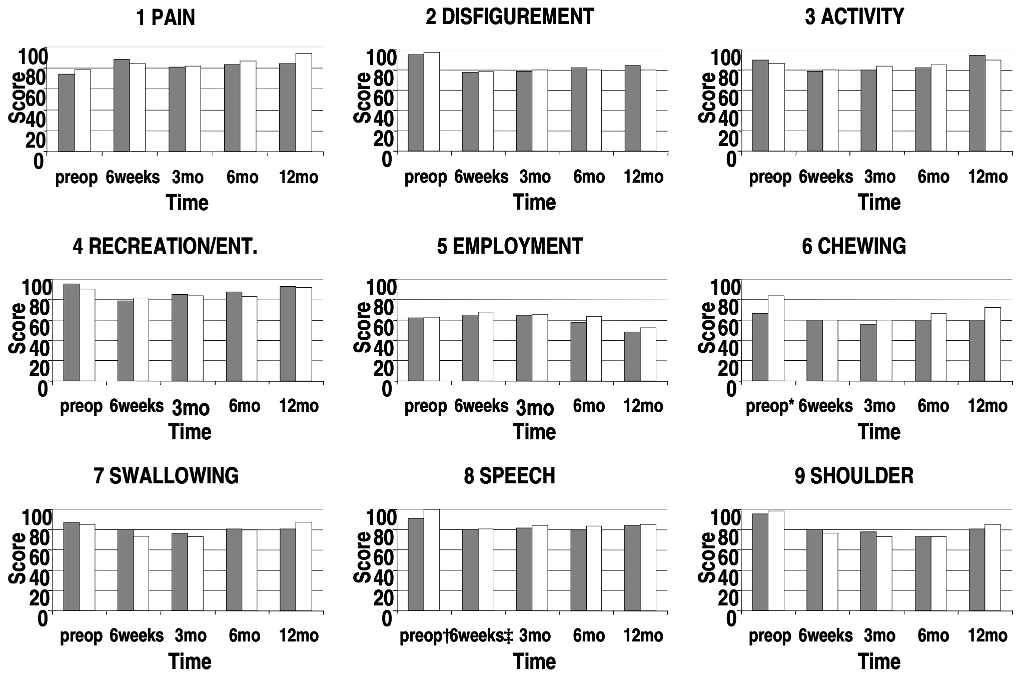


Figure 2. UWQOL domain scores to 12 months in patients with oral cavity (OC, grey columns) or oropharyngeal (OP, white columns) tumor. No. of OC pts: PREOP (n =23), POST6wk (n = 18), POST3mo (n = 18), POST6mo (n =17), POST12mo (n = 13). No. of OP pts: PREOP (n = 15), POST6wk (n = 13), POST3mo (n = 11), POST6mo (n = 12), POST12mo (n = 10). Differences of the absolute domain scores, and the changes in the domain scores from the PREOP value between OC and OP patient groups were examined by the Mann-Whitney U test. *, PREOP, better score for OP than OC pts ($p < 0.05$). †, PREOP, better score for OP than OC pts ($p < 0.01$). ‡, POST6wk, greater decline from PREOP level in OP than OC pts ($p < 0.05$).

5.3 Speech (III, V)

The patient-rated intelligibility (Sp-UWQOL) deteriorated significantly after operation and maintained this level thereafter (see Speech, Table 6). In Study III, the instrumental assessment of the prerequisites for sound speech physiology, i.e., VP closure, nasalance, and nasal airway, pointed out that these variables were normal before operation (see Study III, Tables 2 through 5, p. 992-993). Postoperatively, OC patients retained their normal speech physiology. OP patients, however, deteriorated in terms of VP closure (range 0.251 – 0.393 cm^2) and nasalance (range 18.6 – 24.2%). Nasal airway in OP patients remained normal after operation. Despite the pathology seen in VP0 of OP patients, their nasalance was normal or close to normal, indicating that the basic elements of speech were maintained, nonetheless, at the group level. Tumor size, stage, sex, and age, and the speech parameters in Study III showed no associations. Constant VP0 for OC and OP patients was detected throughout postoperative one year, indicating that RT may not further impair VP0, which is in line with another study (Seikaly and Rieger, et al., 2003).

Results of the perceptual analysis of articulatory and voice characteristics (Study V) are presented in Fig 3. Misarticulations of /r/ and /s/ increased significantly or very significantly (McNemars's test) after operation but virtually collapsed into the mildest error type only, i.e., distortions. Association of misarticulation of /r/ was analyzable with the medical, sociodemographic, and surgical group variables only preoperatively, because of the paucity of normally articulated /r/ after therapy. No relationships were detected before operation. Misarticulation of /s/ was also analyzed against the same group variables. No significant relationships emerged pre or postoperatively. The group sizes being too small made determination of the influence of tumor size and stage on misarticulation of /s/ infeasible. A negligible effect of these tumor features is suggested, because, preoperatively, misarticulated /r/ and /s/ occurred significantly less often in patients with a primary tumor than in OC and OP patients who had previously undergone smaller resections ± RT for oral cancer and now presented with tumor recurrence. After therapy, misarticulated /r/ and /s/ manifested equally in primary and in recurrent tumor groups.

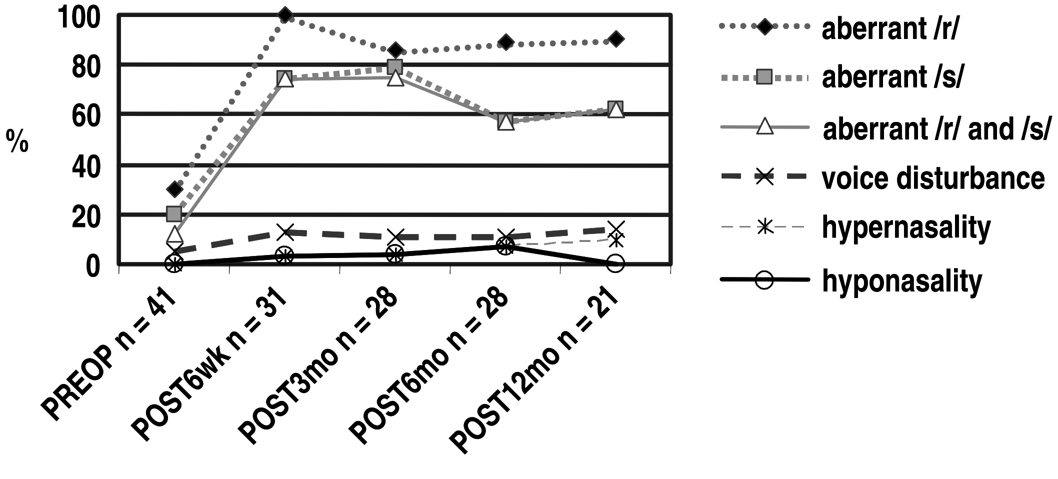


Figure 3. Incidence (%) of articulation and voice characteristics in OC and OP patients to 12 months.

Before operation, Sp-UWQOL was significantly related to misarticulations of /r/ and /s/, indicating superior subjective speech intelligibility in the absence of deviant /r/ and /s/. Similar correlation was shown with Sp-UWQOL and articulation of /s/ after treatment, this relationship being significant at POST6wk and POST12mo but insignificant at POST3mo, and POST6mo despite the same trends. Sp-UWQOL was similar for OC and OP patients after therapy.

Distortion of the sound /l/, hyponasality of /m/ and /n/, substitution of /t/, and compensatory articulation occurred occasionally, but no more at POST12mo.

VP insufficiency resulted in perceptually recognizable mild distortion of one of the pressure consonants in 14.6% of the patients. Speech resonance and voice quality remained basically normal throughout the study. These variables in Study V were not examined against the medical, sociodemographic and surgical variables. About 90% of the patients had undergone neck dissection and RT. The influence of these treatment components on misarticulations, voice quality, and speech intelligibility were not analyzed. Almost invariably, oral cancer patients receiving RT develop xerostomia, which aggravates speech (Chambers and Garden, et al., 2004). Surgical removal of the primary tumor may result in substantial damage of the supra and infrahyoid musculature. The biomechanical imbalance in the muscular strength may lead to disturbances in voice quality with respect to fundamental frequency, intonation and ultimately decreased modulation and practicability (Zimmermann and Sader, et al., 2003). Selective or modified radical neck dissections spare functionally important structures, which may promote voice maintenance.

Methodology of the speech assessment varies greatly in previous studies (Hara and Gellrich, et al., 2003a; Seikaly and Rieger, et al., 2003; Nicoletti and Soutar, et al., 2004b; Borggreven and Verdonck-de Leeuw, et al., 2005). Typical specific speech outcomes have not yet been determined. Tumor size has been shown to negatively influence the consonants errors, /k/, /s/, /d/, and /t/ being the most difficult sounds (Borggreven and Verdonck-de Leeuw, et al., 2005). The quality of the voiceless fricative segments in /s/, /sh/, /f/, and /th/ was not related to the resection size for tumors in the floor of the mouth or the retromolar trigonum (Nicoletti and Soutar, et al., 2004b). For tongue tumors, the resection size and consonant quality were significantly related (Nicoletti and Soutar, et al., 2004b). In the OP, the resection volumes of the base of the tongue were not associated with word or sentence intelligibility (Seikaly and Rieger, et al., 2003). Word intelligibility was not related to resection site, OC vs. OP, or the flap in another study (Hara and Gellrich, et al., 2003a), either.

After being treated for H&N cancer, patients rank their speech as being highly important for them (Rogers and Laher, et al., 2002). Poor speech function has been shown to predispose these patients to dropout from all causes, which may adversely influence the validity of the results in a longitudinal study (Colangelo and Logemann, et al., 1999a,b). Speech and speech related physiologic functions were examined instrumentally and perceptually (III, V) from various speech tasks. The instrumental methods measuring nasalance (Haapanen, 1991; Hardin and Van Demark, et al., 1992; Dalston, Neiman, and Gonzalez-Landa, 1993) and speech aerodynamics (Warren and Dubois, 1964; Warren, 1979; Andreassen, Smith, and Guyette, 1992; Zajac, 2000) are widely used and accepted in patients with congenital or achieved dysmorphology of the oral apparatus (Warren, 1986; Laine and Warren, et al., 1988; Dalston, Warren, and Dalston, 1991; Hardin and Van Demark, et al., 1992; Hinton and Warren, 1995; Seikaly and Rieger, et al., 2003; Searl and Evitts, 2004) as well as in normal speakers (Dalston, Warren, and Smith, 1990; Andreassen, Smith, and Guyette, 1992; Zajac and Mayo, 1996; Dotevall and Lohmander-Agerskov, et al., 1998; Zajac, 2000), or in artificial conditions

(Huber, Stathopoulos, and Sussman, 2004). The results in this study reflected excellent internal consistency indicating reliability of methods used. Perceptual speech judgement is regarded as an important outcome measure of oral functions after surgical interventions. Some aspects have to be adduced, however, to consider the validity of perceptual ratings. Perceptual speech analysis does not identify the organic defect. Neither does it represent the instrumentally documented physiology of oral function. Additionally, perceptual methods are accentuated in literature because speech medicine is in fact practised in only a few countries. This means that the majority of speech examiners are not medically educated, which limits their examination repertoire. Because of differences in the education and background of humanists and physicians, their viewpoints in the interpretation of data differ also. It is also pointed out that perceptual speech assessment is always subjective. Moreover, in the case of judging many different speech parameters, ratings between naïve and trained listeners may show marked variability (Chan and Yiu, 2002). Even experienced judges may vary in their ratings (Keuning, Wieneke, and Dejonckere, 1999; Zraick, Wendel, and Smith-Olinde, 2005). It is important that surgical treatment is considered in relation to organ-based findings, not just functional symptoms. It is, however, recommended that impairment-based-only methods be developed into outcome measures that incorporate more of the functional issues that affect the quality of life (Sell, 2005).

With the combination of instrumental and perceptual measurements, we wanted our study to fulfil the general requirements of a comprehensive speech assessment. The validity of speech rating has been shown to improve along with experience and academic training (Lewis, Watterson, and Houghton, 2003). Both listeners in this study were highly academically trained and experienced, and their rating demonstrated high interrater agreement. The results of instrumental and perceptual analyzes in this study showed excellent internal consistency confirming the validity and reliability of the methods used.

5.4 Swallowing (IV)

The current goals of tumor management include re-establishment of normal food intake and safe swallowing. Fig. 4 presents the radiologist-rated summary of the VFG (VFGR) and the patient-rated swallowing ability (Sw-UWQOL), which correlated strongly with each other. The deterioration in both measures was significant after operation except that of Sw-UWQOL at POST12mo (Table 6) (Wilcoxon signed-rank test). VFGR and Sw-UWQOL were unrelated to the selected medical, sociodemographic, and surgical variables. The percentage of patients able to resume a regular masticated diet PREOP, and at POST6wk, POST3mo, POST6mo, and POST12mo was 69%, 32%, 26%, 50%, 52%, respectively, with 6 and 12-month results being not significantly less than before operation. POST12mo, all but one patient (98%) were on oral diet.

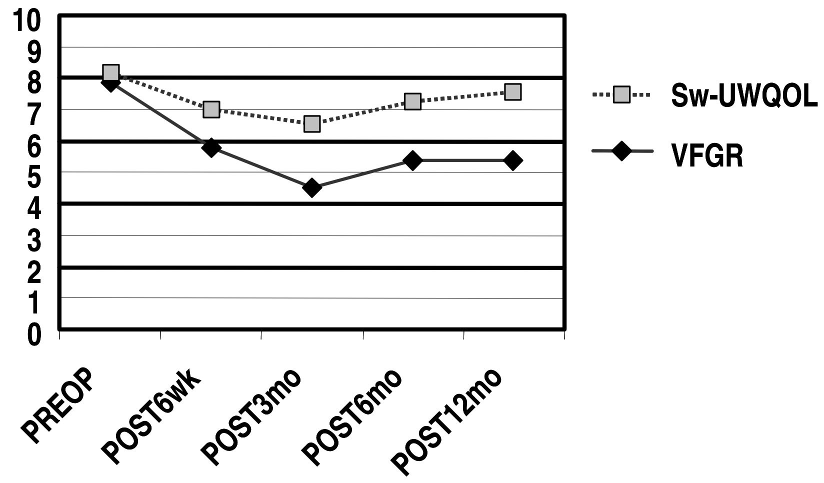


Figure 4. Patient-perceived swallowing (Sw-UWQOL) and videofluorography report (VFGR) in OC and OP patients to 12 months. No. of pts in Sw-QOL: PREOP (n = 38), POST6wk (n = 31), POST3mo (n = 28), POST6mo (n = 28), POST12mo (n = 21). No. of pts in VFGR: PREOP (n = 39), POST6wk (n = 31), POST3mo (n = 31), POST6mo (n = 28), POST12mo (n = 21).

After operation, the analysis of the swallowing sequence with the VFG showed that all observation points, both oral and pharyngeal, indicated impairment. The impairment in all these measures was significant at POST3mo. At POST12mo, oral phase was still worse than before operation, but the difference was no longer statistically significant. Pharyngeal phase remained, however, significantly below the preoperative level of function, except in terms of laryngeal elevation. Fig. 5 presents incidents of abnormal swallowing during the follow-up. For vestibular penetration of the contrast media, the incidence remained significantly elevated throughout the postoperative follow-up. Tracheal aspiration and silent aspiration reached significantly elevated incidence rates from POST3mo onwards, and at POST12mo, respectively (McNemars's test). Chronic pulmonary changes, which were not identifiable PREOP were detected in 3 (15%) patients POST12mo. All of them aspirated as well. Aspiration was uncorrelated with the selected medical, sociodemographic and surgical group variables. PREOP, 13% of the patients aspirated, 83% of them silently. At the end of the follow-up, 52%of the patients reported eating regular food, 36% of them aspirated with an 18% rate of silent aspiration. Of all patients at 12 months, 44% aspirated, 70% of them silently. Their overt aspiration was significantly related to the self-perceived swallowing ability, whereas silent aspiration was not.

The mechanisms underlying aspiration are not fully understood (Smith and Logemann, et al., 1999; Jafari and Prince, et al., 2003; Ramsey, Smithard, and Kalra, 2005). Treated or untreated, H&N cancer is a known cause of overt and silent aspiration (Smith and Logemann, et al., 1999; Stenson and MacCracken, et al., 2000). Prevalence of silent aspiration varies in previous reports, depending on the medical diagnoses, and can be as high as 94% (Smith and Logemann, et

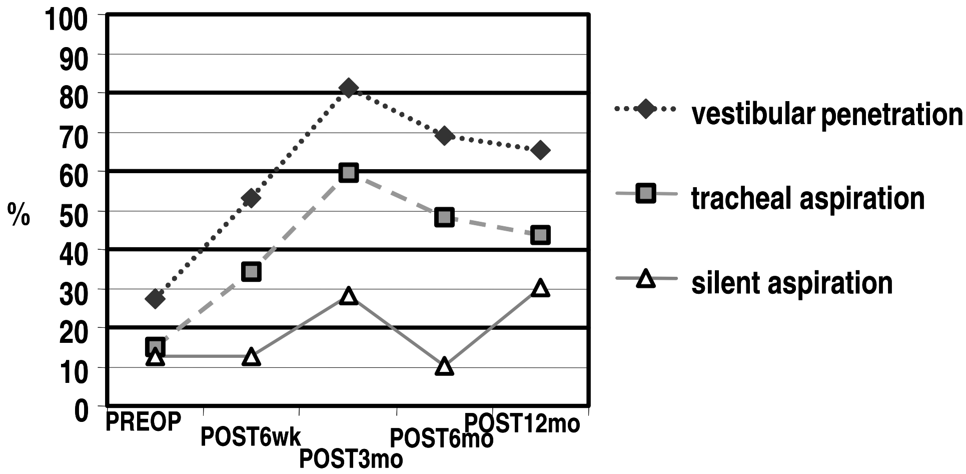


Figure 5. Incidence (%) of vestibular penetration, overt and silent aspiration of the contrast media in OC and OP patients to 12 months. No. of pts: PREOP (n = 39), POST6wk (n = 31), POST3mo (n = 31), POST6mo (n = 28), POST12mo (n = 21).

al., 1999; Ramsey, Smithard, and Kalra, 2005;). Any damage causing aspiration can result in overt or silent aspiration (Smith and Logemann, et al., 1999; Mittal and Pauloski, et al., 2003). Patient characteristics predisposing to silent aspiration among oral cancer patients, apart from UADT cancer per se, include chronic gastroesophageal reflux, prolonged intubation or ventilation, tracheostomy, older age, cerebrovascular disease, diabetes, and previous myocardial infarction (Ramsey, Smithard, and Kalra, 2005). Incidences of overt and silent aspiration increased in the present study. It is difficult to point out the postoperative factor responsible for this. These results may reflect the study protocols and may not be directly comparable with others (Logemann and Pauloski, et al., 1993; Pauloski and Logemann, et al., 1993; Pauloski and Rademaker, et al., 2000; Pauloski and Rademaker, et al., 2004).

Detailed comparison of VFG between OC and OP patients demonstrated that OC patients were better able to swallow. However, OC and OP patients were similar in relation to aspiration (overt or silent), VFGR, Sw-UWQOL, and in their ability to eat regular food. It is concluded that cancer therapy including free flap reconstructions and RT in the OC or OP cause clinically uniform changes in swallowing irrespective of tumor site or stage. Accumulation of reported swallow outcomes after free flap reconstruction is yet deficient. It has been suggested, based on populations including OC or OP free flap patients, that surgical variables such as posterior resections, increasing percentage of tongue base removed, and disparity between the resection and reconstruction volumes negatively influence swallowing (Pauloski and Logemann, 2000; Hara and Gellrich, et al., 2003b; Seikaly and Rieger, et al., 2003; Nicoletti and Soutar, et al., 2004a; Pauloski and Rademaker, et al., 2004).

The method used for rating swallowing was VFG, which is regarded by many as the “gold standard” in swallow assessment, despite problems with its reliability

(Ramsey, Smithard, and Kalra, 2005). Study IV focused on determining success in attaining a regular masticated diet. Particular causes of aspiration, such as premature spillage of the oral contrast media into the hypopharynx, or delayed clearance of contrast media from the hypopharynx, were not analyzed, nor were aspiration per swallow, the percentage of bolus aspirated, or the influence of various bolus consistencies on aspiration. Some patients received swallowing therapy the association of which was not analyzed in relation to swallowing. Changes in patient weight were not measured.

5.5 Sensation (IV, V)

Fig. 6 demonstrates the anterior intraoral sensation to 12 months. The recipient nerve was the greater auricular nerve in 25/27 (93%) patients. Sensation weakened significantly after operation as could have been expected from earlier studies (Aviv and Hecht, et al., 1992; Bodin, Jaghagen, and Isberg, 2004) (Wilcoxon signed-rank test). Sensation and the medical, sociodemographic, and surgical group variables, as well as the speech variables (misarticulation of /r/ preoperatively or of /s/ pre or postoperatively, Sp-UWQOL) and swallowing variables (VFGR, aspiration, silent aspiration, or Sw-UWQOL) showed only coincidental statistically significant relationships, which were regarded as clinically insignificant. This study could not demonstrate any association between oral function and intraoral sensation. Superior sensation has been suggested to be obtainable by selecting a recipient nerve with more extensive nerve representation in the sensory cerebral cortex, such as the lingual nerve (Santamaria and Wei, et al., 1999; Urken, 2004), but whether this would improve function, is not known.

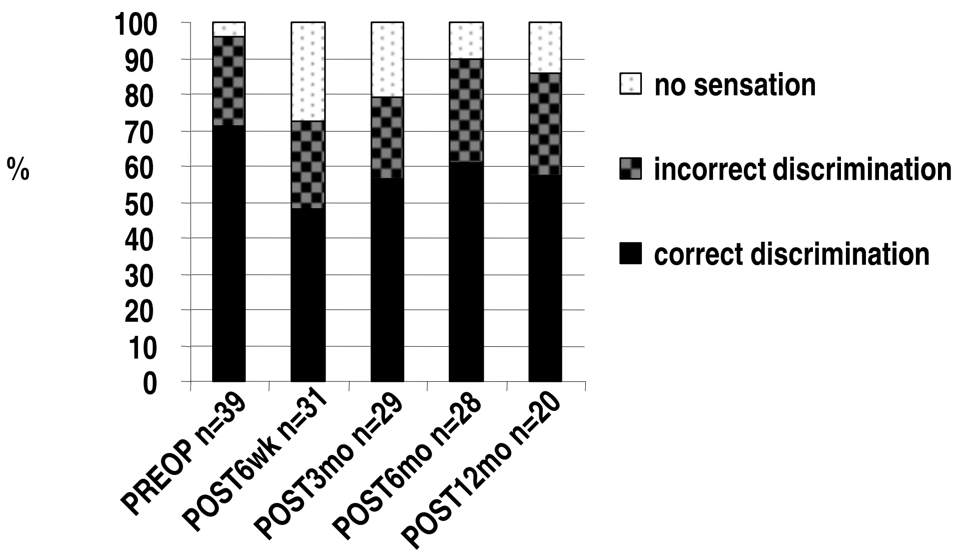


Figure 6. Sensation in OC and OP patients to 12 months.

Intraoral sensation was examined for its relationship to swallowing and speech by a single simple method, 2-point moving discrimination (IV, V). The areas tested included 4 anterior sites. Reconstruction flaps were innervated whenever feasible (61%). The follow-up study was not primarily designed to differentiate the sensation outcome or any other outcome between innervated and non-innervated flaps. Such studies would have necessitated several methods for assessing sensation, randomization and double-blindness during the follow-up tests.

6 General discussion and conclusions

Oral and pharyngeal cancer has worldwide significance and could be mainly avoided through lifestyle alteration. Despite extensive advancement in cancer study and achievements in cancer management, survival after these cancers still remain limited when compared to many other types of malignant diseases. As with cancer in any part of the body, oral or pharyngeal cancer and its treatment cause a life-altering concern for all those involved. The treatment of these tumors may endanger the functions that are essential and vital for anyone, breathing, speaking, chewing and swallowing. Treatment success is easily observable by other people. Moreover, deviating appearance may substantially reduce the subjective and objective social acceptance of a person. The present knowledge of treatment outcomes following large intraoral cancer resections combined with free tissue reconstructions mainly derives from studies discussing survival and surgery-related complications. Modern surgery needs to become more functionally oriented, which necessitates studies on function and quality of life before and after treatment.

In this study, a population of 50 oral and pharyngeal cancer patients were analyzed in retrospect (I), and another 44 in a prospective (II-V) manner. The 50 oral and pharyngeal cancer patients were analyzed for survival and complications after free flap reconstruction with or without radiotherapy (I). The 44 similar patients were prospectively followed-up and assessed for survival (II), complications (II), speech (III, V), swallowing (IV) and quality of life (II), preoperatively, and at 4 time points during a 12-month period.

The previous comprehensive literature reports rather limited survival rates after oral and pharyngeal cancer and susceptibility for these cancers to recur. Our study demonstrates consistency with the previous results on the overall (3-year OS 42% and 45%) and disease-free (1-year DFS 43%) survival. Lethality of these tumors refers to the fact that oral malignancies often become diagnosed at a locally advanced stage (Scully and Porter, 2000). Furthermore, recent understanding of molecular level events has brought evidence of the multistep and multifocal mechanisms underlying oral carcinogenesis. Every measure should be exploited in the prevention of oral and pharyngeal cancer. No doubt, further improvement in cancer imaging techniques, education, and research, all contributing to the early detection and screening of oral cancer will finally lead to better prognosis of these frightening diseases.

Surgical management of oral or pharyngeal cancer combined with free flap reconstruction is regarded as a major surgery with lengthy operative times and substantial blood loss. Considering major surgery, these cancer patients present with several risk factors. Cancer per se causes an operative risk. It is common for an oral cancer patient to suffer from a comorbidity. Aging influences several organ systems, reducing their tolerance to operative stress. Many patients are heavy smokers and drinkers and may be afflicted by a yet undiagnosed disease that would have necessitated regular medical attendance. Poor nutritional status is common. Referring to the aforementioned patient characteristics, complications (rate for all complications, 58% and 66%) after major surgery in this study must be considered partly unavoidable. These results are in line with other studies. Excellent flap success (96% and 98%) and low frequencies of reoperation and fistula rates are representatives of high standard surgical technique. The high perioperative mortality rate (11%) and shorter survival in Study II are suggested to refer to unemployment, heavy drinking and smoking. This result is believed to hold clinical relevance. It could be beneficial if, in the preoperative screening and counseling of the oral or pharyngeal cancer patient awaiting microvascular reconstruction, special emphasis would be engaged to these sociodemographic factors along with searching for other operative risks.

Quality of life deteriorated after treatment in terms of the global quality of life score, which did not improve significantly during the follow-up. This indicates that extensive resection of oral or pharyngeal cancer combined with free flap transfer and radiotherapy may not result in ideal quality of life. Closer inspection of the domain scores reveals that the domains measuring appearance, chewing, speech, and shoulder function remained significantly below the preoperative level during the follow-up. This is consistent with other studies in which patients tend to rate the UADT functions and social acceptance as highly important for them (Rogers and Laher, et al., 2002b; Rogers and Lowe, et al., 2002; Millsopp and Brandom, et al., 2005). The result also highlights the importance of the functional outcome of the treatment. We demonstrated significant associations between quality of life outcome and sociodemographic variables. There would be a need for a short comprehensive instrument for use in clinical practise with a cut-off score, so that the quality of life issue could easily be discussed with the patient and that those adversely affected could be directed to rehabilitation (Bjordal, 2004).

The importance of speech for an individual remains unequivocal in this study. The basics for normal speech, i.e. balanced speech aerodynamics, could be maintained by the present treatment protocol. After resection and reconstruction of the oral pharynx, however, several patients demonstrated enlargement of the velopharyngeal orifice size. This was not indicated to be clinically relevant, because in this patient group, speech was normal in terms of nasality, perceptually or instrumentally measured. It indicates probably that the enlarged VP orifice was aeromechanically compensated. Articulatory ability of the sounds /r/ and /s/, however, was reduced significantly, which was strongly related to the patient-perceived intelligibility of his/her speech. The results concerning articulation were not related to clinical variables, which leads to the conclusion that surgical intervention in the oral cavity or oropharynx, with very high probability, causes an articulatory impairment that is difficult for the patient. Although the articulatory errors of /r/ and /s/ were almost without exception of the mildest type, which alone should not interfere with even the most demanding speech tasks, the problem in the current patient population involves greater complexity. The cumulative influence of several articulatory deviances, resonance disturbance, voice impairment, xerostomy, which may cause a fricative sound in speech, loss of speech fluency, reduced modulatory ability of speech, and eventual drooling, may reduce the aesthetics and the social acceptance of speech. Surgery should develop towards practices that spare or enable oral functions. Despite the importance of functional speech and the high frequency of speech problems in oral cancer patients, the low referral rate to speech therapy is surprising (Radford and Woods, et al., 2004). The role of speech rehabilitation is strongly indicated to support cancer patient.

Swallowing impaired after the present therapy. Discrepancy occurred between the swallowing ratings by the radiologist and by the patient him/herself. One year after treatment, 98% of the patients at this time point had achieved oral nutrition. Of the patients, 52% were capable of consuming a regular masticated diet. Unsafe swallowing, however, was often encountered. At 12-month swallow examination, 44% of the patients aspirated, 70% of whom silently. Pulmonary changes referring to aspiration and unsafe swallowing occurred in 15% of the patients one year after operation. Overt and silent aspiration was diagnosed preoperatively, and throughout the follow-up. It is concluded that hazard of swallowing should be routinely, regularly tested with various bolus consistencies, and rehabilitated, irrespective of the patient's perception of swallowing ability.

Sensation was not the main focus in this investigation. With the present study design, in which there was 61% innervation frequency of the reconstruction flaps (the great auricular nerve being the recipient nerve in most flaps (93%)), sensation and the oral functions of speech and swallowing were unrelated. This finding does not support the necessity for flap innervation in order to establish improved oral function.

Modern surgery acknowledges the importance of oral functions. Surgery should continue to make progress in this area, and methods that lead to good functional results should be developed. Operational outcome should always be evaluated in terms of function. The mouth and the pharynx encompass a unit of utmost functional complexity.

The conclusions of this study are the following:

1. Survival after resection and microvascular free flap reconstruction of extended oral cavity or pharyngeal cancer indicated a fair outcome with a 3-year overall survival of 42% and 45%.

2. Postoperative complications occurred frequently, in 58% and 66% of the patients.

3. The present therapy did not result in subjectively perceived optimal quality of life compared to the preoperative values, especially in the domains measuring appearance, chewing, speech and shoulder function.

4. Patient-perceived speech intelligibility was reduced, despite the maintenance of the sound prerequisites for producing normal speech. Incidence of individual misarticulations increased quite substantially, but transiently. In the latest expert ratings, the speech quality was not negatively affected by many types of errors. However, the misarticulations of the /r/ and /s/ sounds were persistent in most of the patients. Hoarseness and hypernasality occurred very infrequently.

5. Oral nutrition was almost invariably re-established. Swallowing was impaired, however, and unsafe swallowing, was diagnosable throughout the study in a significant number of patients, and was unrelated to patient-perceived swallowing ability.

6. Intraoral sensation deteriorated, which was unrelated to speech and swallowing ability. Innervated flaps proved no superiority with respect to function.

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